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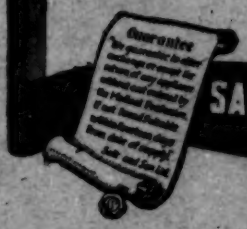

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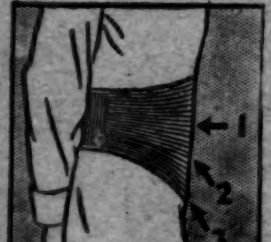

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JANUARY 27 1945

THE ACTION OF PENICILLIN ON BACTERIA

BY

LAWRENCE P. GARROD, M.D., F.R.C.P.

Bacteriologist to St. Bartholomew's Hospital; Professor of Bacteriology in the University of London; Pathologist, E.M.S.

ulphonamides had been in general use for five years before e nature of their action on bacteria was discovered. The istory of penicillin is developing on similar lines: so remark- le were its properties as demonstrated by *in vitro* and animal periment, and so encouraging to clinical trial, that the treat- ent of human disease was embarked on at an early stage, d has engrossed almost all attention. The far-reaching success f these efforts does not diminish the need for a clearer under- nding of how penicillin acts on bacteria: such knowledge ay indeed enable clinical treatment to be directed even more ffectively.

In the first full description by Florey and his colleagues braham *et al.* 1941) observations on the persistent respira- n and survival of staphylococci exposed to penicillin are entioned in support of the view that its action is bacterio- atic rather than bactericidal. By performing viable counts bacteria exposed to the action of penicillin Hobby, Meyer, d Chaffee (1942) and Rammelkamp and Keefer (1943) showed t a great diminution in the number of living cells occurs, ten ending in extinction, although a small proportion of sur- vors may persist. Similar experiments by Rantz and Kirby 944) led them to state unequivocally that penicillin is bac- ricidal. Bigger (1944b) has reached the same conclusion, but alifies it by advancing the hypothesis that this lethal action exerted only against bacteria which are about to divide. The me idea has been put forward with similar supporting evi- nce by Hobby and Dawson (1944) and by Miller and Foster 944).

Up to now no author appears to have examined penicillin the methods usually applied to ordinary disinfectants. It true that penicillin is far from being ordinary, but, on the her hand, if it is a disinfectant, as some of these findings ggest, an accurate knowledge of the influence on its action the various factors which are known to control chemical sinfection generally might well be helpful. This was the aim some of the following experiments.

Method.—The only organism used was *Staphylococcus aureus* xford H strain), of which such an amount of a 24-hour broth lture was added to the test mixture as to give a concentration of om 25,000 to about 5,000,000 viable cocci per ml. The medium ually broth), the concentration of penicillin (added as a distilled- ter solution in a small volume), and the temperature were varied stated later. Survivors were counted at intervals in pour agar ates from 1 in 10 to 1 in 10,000 dilutions, penicillinase made by gar's (1944) method being added if necessary.

Bactericidal Action

It has been shown by others, and is evident from the follow- g experiments, that penicillin causes the death of bacteria der favourable conditions fairly rapidly. I was not at first clined forthwith to accept this as evidence of true killing, cause bacteria kept at 37° C.—a necessary condition for the pid penicillin effect—and merely prevented from multiplying, ether by a mechanism involving deprivation of nutriment or herwise, will certainly not survive long. It might appear mple to settle this point by employing a non-nutrient medium, t in my hands the death rate at 37° C. of washed staphylo- cci in different batches of Ringer's solution made with ss-distilled water varied inexplicably, and although usually celerated by penicillin, was once (by a different sample) clearly retarded. To distinguish between bactericidal and bac- teriostatic action also demands a definition of these terms; which is to be used of a substance that inhibits an essential metabolic process and thus causes ultimate death by starvation? The distinction, in terms of effect, can only be a matter of time, and later observations have convinced me that the peni- cillin effect is far too rapid in some circumstances to be regarded as anything but bactericidal.

The Effect of Concentration

An increase in concentration accelerates the action of all common disinfectants. The reverse is often true of penicillin: in the experiment illustrated in Fig. 1 death was much more

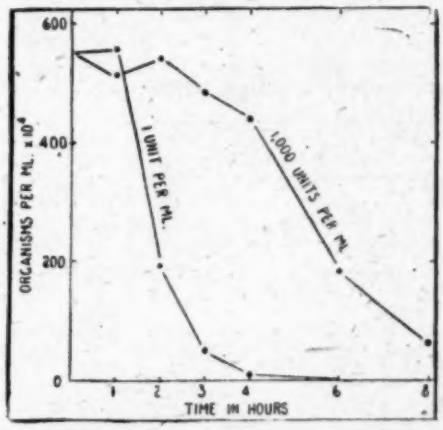

FIG. 1.—Numbers of surviving *Staph. aureus* in broth at 37° C. containing penicillin (TRC10) in concentrations of 1 unit and 1,000 units per ml.

rapid in the presence of only 1 unit per ml. than with 1,000 units. This result is an example of those obtained in many experiments, three of which are expressed, for the sake of brevity, in a different form in the following Table. The LT50 (Withell, 1942) is the time required to kill 50% of the inoculum, and, since the survivor curve in the presence of penicillin in any given medium is of constant shape, this value fairly reflects the rate of disinfection.

LT50 in Minutes for 3 Different Penicillins in 4 Concentrations in Broth at 37° C.

Penicillin	Potency (Units per mg.)	Concentration of Penicillin (Units per ml.)			
		1	10	100	1,000
TRC8	30	105	111	258	195
TRC10	100	106	118	152	318
"Pure"	1,360	100	91	89	95

The first two samples were of early manufacture and contained a high proportion of impurities: both are most active in the lowest concentration—1 unit per ml.—and least active in one case in that of 1,000 units and in the other of 100. "Pure" penicillin, on the other hand (actually of about 85% purity), disinfects at an almost constant rate regardless of concentration within this range: the differences observed are within

the limits of error of the method. It seems probable that above a certain necessary minimum the rate of disinfection by pure penicillin is unaffected by increase of concentration. On the other hand, something—presumably impurities—actually retards disinfection when the concentration of impure material is increased. That this does not apply only to samples of very low potency was shown by a similar experiment with a recent commercial product (Pfizer) of high potency (about 1,050 units per mg.). In concentrations of 0.1, 1, 10, 100, and 1,000 units per ml. there were less than 4% of survivors after 2 hours, but in 10,000 units per ml. there were 34%.

The effect of smaller variations in a lower range was also tested. In the following experiment each concentration is one-quarter of the preceding:

LT50 in Minutes for 2 Penicillins in 5 Concentrations in Broth at 37° C.

Penicillin	Concentration of Penicillin in Units per ml.				
	10	2·5	0·62	0·15	0·039
TRC10	92	118	118	148	>480
"Pure"	110	102	114	130	>480

There is in either case no significant difference between the rates of disinfection in the three higher concentrations: retardation is slight in 0.15 unit per ml. and marked in 0.039. A similar experiment in human blood (inactivated at 50° C. for 15 minutes), using TRC25 (360 units per mg.) in concentrations of 10, 5, 2, 1, 0.5, 0.2, and 0.1 unit per ml., gave values for LT50 of 58, 70, 75, 88, 108, 140, and 174 minutes respectively. Although these figures suggest that raising the concentration accelerates disinfection, there is less difference at a later stage: at 4 hours the percentage of survivors in all concentrations was under 3, showing that in this medium disinfection is accelerated only in its early stages by increase in concentration.

The Effect of Temperature

The action of all chemical disinfectants is accelerated by increase in temperature, and penicillin is no exception (Fig. 2)

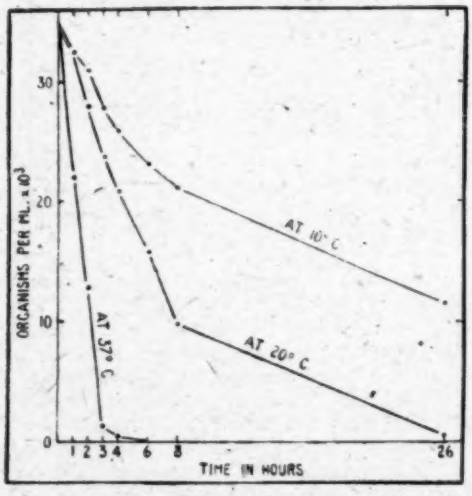

FIG. 2.—Numbers of surviving *Staph. aureus* in broth containing 10 units per ml. of penicillin at 10°, 20°, and 37° C.

The degree of this acceleration (i.e., the temperature coefficient) varies among different classes of disinfectant, and appears to be by no means so extreme for penicillin that it can be used to support the argument that this drug has a peculiar type of action. Bigger (1944b) believes that penicillin kills only dividing cells, and cites its inactivity at low temperatures in support of this; it is, in fact, slowly bactericidal not only at 10° C., as shown in Fig. 2, but at 4° C. This was demonstrated in another experiment, in which a 50% reduction in the viable count was observed in 2 days and 100% in 14. Disinfection by penicillin was also further accelerated as compared with that at 37° C. by raising the temperature to 42°. This is characteristic of an ordinary disinfectant, and not what would be expected according to Bigger's hypothesis, since at this temperature growth ceases. Further observations of the action of penicillin at this or even higher temperatures might be instructive.

The Effect of *p*H

Penicillin, although rapidly destroyed by strong acids, is stable to be stable between *p*H 7.0 and 5.0. That it is not equally active throughout this range of acidity is shown in Fig.

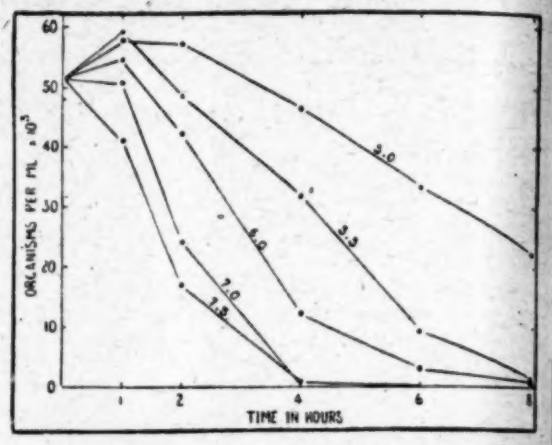

FIG. 3.—Numbers of surviving *Staph. aureus* in broth adjusted to *p*H 7.5, 7.0, 6.5, 6.0, 5.5, and 5.0, and containing 10 units of penicillin per ml. at 37° C. (The curve at *p*H 6.5 is almost identical with that at 7.0, and is omitted. Slow multiplication occurred in control broth at *p*H 5.0 with no penicillin.)

which illustrates the rate of disinfection by 10 units per ml. of penicillin in broth adjusted to six different reactions by the addition of HCl (all were diluted to the same extent by making up to constant volume with distilled water). The experiment was suggested by an anomalous result in an attempt to confirm the observation of Abraham *et al.* (1941) that penicillin acts as well in pus as in blood, serum, or broth. The pus used contained only an anaerobic streptococcus; a standard staphylococcus was added to it. Disinfection proved to be much retarded relative to that in control media (broth, serum, and blood), and a possible cause for this was found when the *p*H of the pus was discovered to be 5.2. A portion was brought to 7.6 and the experiment repeated with broth: at 5.2 the LT50 was still over 4 hours; at 7.6 it was under 2. A low *p*H in an inflammatory exudate may therefore impair the action of penicillin: this factor is worthy of study as a possible cause of failure in treatment.

The Effect of Reproductive Activity

The suggestion recently made by various authors that penicillin kills only dividing cells prompted several experiments some of which support this conclusion in part, while others do not. Their results are here stated briefly:

1. Action in Diluted Broth.—According to Bigger, the viable count of staphylococci in 1 in 800 broth remains stationary. The medium supporting life but not growth, and penicillin in this medium is inactive. When the LT50 for 10 units of penicillin per ml. in undiluted broth at 37° C. was 103 minutes, it was 208 minutes in 1 in 800 broth: the population remained stationary in a 1 in 800 broth control during this period, but increased subsequently. In another experiment with a different broth, in which very little late growth occurred, the LT50 in 1 in 800 medium was 335 minutes. This medium therefore does reduce the rate of disinfection; it by no means prevents it.

2. Presence of Another Bacteriostatic Agent.—Bigger found that boric acid, which is bacteriostatic, prevented the bactericidal action of penicillin. I have tried two other such agents. Proflavine in low concentrations is bacteriostatic for staphylococci and only slowly bactericidal. The LT50 of 1 in 90,000 proflavine in broth at 37° C. was 215 minutes, that of 10 units of penicillin per ml. 92 minutes, and that of both combined 165 minutes. Proflavine therefore does reduce the activity of penicillin, but this may possibly be due to chemical incompatibility. The ideal purely bacteriostatic agent appears to be a sulphonamide: the results of an identical experiment

sulphathiazole are given in Fig. 4. Sulphathiazole in a concentration which almost completely prevents growth somewhat reduces the rate of disinfection by penicillin.

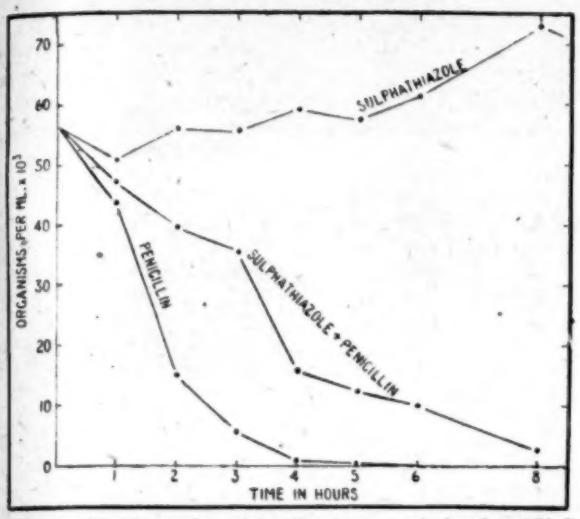

FIG. 4.—Numbers of surviving *Staph. aureus* in broth at 37° C. containing (1) 0.2% sulphathiazole; (2) 10 units penicillin per ml.; (3) both of the drugs.

3. Age of Culture.—If reproductive activity is an important factor there should be a marked difference in the action of penicillin on old and that on young cultures. In this there would be nothing unique: young cultures are more susceptible to disinfectants generally than old, and this is recognized in the stipulation that a culture of prescribed age shall be used for any standard test. Nevertheless it seemed worth while to study this factor, and the behaviour of a culture 10 days old (for 9 of which it had been on the bench) was compared with that of one 5 hours old (i.e., in the logarithmic phase of growth). Previous viable counts on such cultures made it possible to add approximately equal numbers of living cells from each to flasks of broth containing 5 units of penicillin per ml. at 37° C. As shown in Fig. 5, the viable count in the young

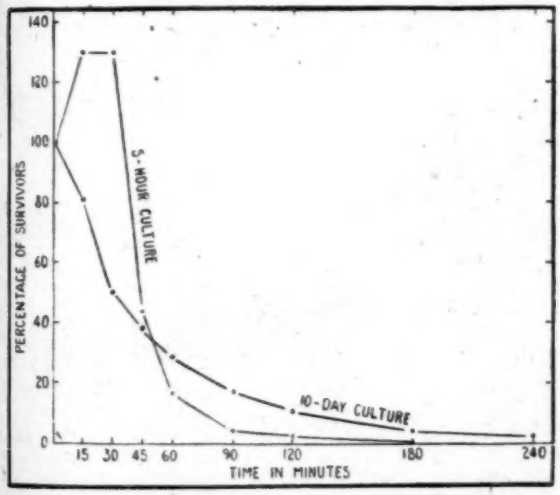

FIG. 5.—Numbers of surviving *Staph. aureus* in broth at 37° C. containing 5 units of penicillin per ml., the organism being derived from a 5-hour-old broth culture and a 10-day-old broth culture respectively.

culture after a slight initial rise fell rapidly; that of the old fell continuously and rather less rapidly; but the rate of disinfection is much the same in both, and lends little support to the idea that a cell is vulnerable only when dividing. Curves similar but for the absence of an initial rise in the young culture were obtained with 1 in 300 phenol controls; the greater resistance of a small proportion of old cells is clearly evident in both. Reproductive activity therefore affects susceptibility to penicillin only in the same way as it affects susceptibility to phenol.

(In this experiment the penicillin broth and the broth for diluting the cultures were brought to 37° C. before the experiment began: this doubtless accounts for the rapid death rate. In other experiments—perhaps unfortunately—the test mixtures were made at room temperature and placed in the incubator or water bath at zero time. They should have reached the required temperature within a few minutes, but Bigger's observations on the effect of cooling suggest that this brief period at a lower temperature may have unexpected effects.)

Discussion

These experiments show that penicillin is fairly rapidly lethal to susceptible bacteria. Beyond that they throw no direct light on the nature of its action. The only other lesson to be learned from them is that further studies of the intimate nature of this action must clearly be pursued with pure reagents. All commercial penicillins tested were less active in high than in low concentrations, and impurities which presumably cause this and other anomalies offer a serious obstacle to such a study. It will indeed be necessary to consider whether pure penicillin itself is a single substance of unvarying composition and uniform action.

On the other hand, some conclusions can rightly be drawn which have a bearing on the clinical use of penicillin as now available. The foremost of these is that nothing is likely to be gained by using high concentrations, particularly for local treatment. Failure of clinical response is usually considered to call for an increased dose, and there is a pardonable belief that the greater the dose the more sure the effect. True as this may be of other therapeutic agents, it is even the reverse of the truth when penicillin is concerned: a concentration of 1 unit per ml. is not only just as effective as one of 1,000 units, but often more so. The only good reason for using strong solutions in local treatment is to ensure that loss by escape, dilution, or absorption shall not permit the concentration to fall below the minimum level for full effect, which may be taken as about 0.1 unit per ml. The factors controlling this loss vary almost infinitely, from good retention in a closed space such as the theca or pleura to the impossibility of retention and the dilution by copious exudate which characterize some open wounds. The optimum strength of solution must therefore vary, but the standard probably need not exceed 250 units per ml.: this was the strength originally employed with satisfactory results for instillation into gunshot wounds after secondary suture by Florey and others in North Africa. That this policy has an additional advantage in economy needs no emphasis.

These experiments also have some practical bearing in relation to Bigger's proposal that systemic penicillin treatment should be intermittent. His argument is that penicillin kills only dividing cells, and that a very small proportion of dormant non-dividing cells which he terms "persisters" are liable to survive: these must be permitted to grow by interrupting treatment if sterilization is to be complete. Of the experiments described here, those using diluted broth and combinations of penicillin with bacteriostatic agents give some support to the idea of a special action on dividing cells. It should be observed in this connexion that Bigger (1944a) has previously recommended combined treatment with sulphathiazole and penicillin: if, as it appears, the action of sulphathiazole as a bacteriostatic agent interferes with that of penicillin, it must detract from rather than add to therapeutic effect. His two ideas of synergic action and bacteriostatic interference are in fact plainly incompatible.

On the other hand, studies of the effect of temperature and particularly of reproductive activity on susceptibility to penicillin demonstrate behaviour which seems to differ in no qualitative sense from that of other disinfectants. While much remains unknown or doubtful, I submit that the evidence for Bigger's hypothesis is inadequate to support so drastic a change in therapeutic policy as he advocates. Clinical experience supports this attitude; the reason for therapeutic failure is to be found not in any property of the micro-organism but in the morbid anatomy of the lesion. Treatment fails in patients with inaccessible foci of infection, such as an area of necrosis in bone, an endocardial vegetation, or an undetected abscess; even those with the severest infections but without such foci regularly recover.

Summary

Penicillin has a bactericidal action.

This action proceeds at a constant rate regardless of concentration within wide limits if pure penicillin is used: impure samples are more effective in low than in high concentrations.

This action is accelerated by increase in temperature throughout the range 4° to 42° C.

The action of penicillin is progressively impaired by an increase in the acidity of the medium between *p*H 7.0 and 5.0.

The behaviour of penicillin in diluted broth and in the presence of bacteriostatic agents supports the hypothesis that it acts only on dividing cells; the effect of temperature and the almost uniform susceptibility of cells from both old and very young cultures are against it.

I am indebted to the Penicillin Clinical Trials Committee of the Medical Research Council for most of the penicillin used, and to I.C.I. (Pharmaceuticals) Ltd. for the gift of 183 mg. of nearly pure penicillin. This work could not have been done without the assiduous technical assistance which was given by Miss P. M. Waterworth. For her services and for the equipment of the laboratory in which the work was done I am indebted to a fund, under the control of Mr. Rainsford Mowlem, which was generously provided by the United States organization "Bundles for Britain."

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PENICILLIN IN GONORRHOEA AND SYPHILIS

WITH NOTES ON TWO CASES OF DUAL INFECTION

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In recent years the widespread use of the sulphonamide group of drugs in the treatment of venereal diseases has had fairly satisfactory results. These drugs have been employed successfully in the treatment of gonorrhoea, soft sore, and other types of non-specific genital ulceration, and lymphogranuloma inguinale. However, from the clinical point of view certain difficulties were early encountered. These were due to the simple fact that a patient presenting the appearances of one venereal disease may well be incubating one or more of the others. Sulphanilamide itself, while almost uniformly successful in clearing an uncomplicated Ducrey infection, is not nearly so effective in the treatment of gonorrhoea. In fact, many cases of the latter infection treated with sulphanilamide developed afterwards a persistent mucoid or muco-purulent discharge due to such complications as anterior folliculitis or a posterior spread. Later a similar effect was seen in certain cases treated with inadequate or "self-administered" doses of sulphapyridine. These cases were extremely difficult to clear up and required prolonged hospital treatment.

The incubation periods of chancroid and gonorrhoea are roughly the same, and in addition a patient may have had more than one recent exposure to infection. Thus a man admitted to hospital a few days after his last exposure to infection and presenting a clinical chancroid might at the same time be incubating gonorrhoea. It became obvious, then, that in such a case the administration of sulphanilamide, while clearing the Ducrey infection, would in all probability mask the signs of the incubating gonorrhoea. In the early days this not infrequently happened. The patient was discharged from hospital with a healed sore and returned in a week or ten days with a persistent urethral discharge showing many pus cells, some secondary organisms, but no gonococci. There was no history of further exposure to infection. This type of case was peculiarly resistant to treatment, and generally one or other of the commoner complications of gonorrhoea was found. This difficulty was obviated by a routine which forbade the use of sulphanilamide in "sore cases" until at least 14 days after the last admitted exposure to infection.

These facts, when realized, are in the main a matter of clinical interest and do not present any serious problem or administrative difficulty. They serve, however, as an introduction to the theme of this short article, which is intended to point out the similar but much more serious difficulties at present attendant on the treatment of sulphapyridine-resistant gonorrhoea with penicillin.

Penicillin is now coming into general use in the treatment of resistant gonorrhoea cases, in which it has been found almost uniformly successful. In the first place, then, it will not be remiss to discuss what we know of its effect on the spirochaete of syphilis, more particularly as many—one might even say most—of the gonorrhoea cases so far treated have been within the incubation period of syphilis—that is, less than three months after the last exposure to infection.

The first observation to be made is on the report from the U.S.A. on 50 cases of early syphilis treated with penicillin, the dose used being 2,500,000 units. The details are not available here. So far as can be gathered, however, *Treponema pallidum* disappeared early from primary lesions, which healed rapidly, and the blood has remained Wassermann-negative for the present period of observation; while in early sero-positive cases there was a gradual reversal of the blood Wassermann to negative. This is as far as the story goes. It is a hopeful report, but we have no means of assessing what will be the ultimate outcome of these cases—i.e., whether this dosage is curative. In this connexion it would be well to remember that penicillin administered intramuscularly or intravenously does not pass into the spinal fluid unless perhaps in minute quantity. Therefore, since invasion of the central nervous system by *T. pallidum* is common in early syphilis, one consideration of vital importance is the possibility that C.N.S. involvement may show an increased incidence.

The second observation is on two cases of sulpha-resistant gonorrhoea recently under our care.

Case I

Pte. X. entered hospital on Sept. 11, 1944. Definite dates of exposure to infection were difficult to obtain accurately (language difficulty). Though he said that the last exposure was approximately seven weeks before admission, the clinical findings suggested a more recent one.

On examination the patient was found to have a purulent urethral discharge and a clinical syphilitic chancre in the coronal sulcus. He stated that the sore had been present for four weeks and the urethral discharge for a shorter period. A urethral smear showed many intracellular gonococci, and the urine was hazy in both glasses. Dark-ground examination showed the sore to be positive to *T. pallidum*. Routine sulphapyridine—27 g. over 5 days—was given, and anti-syphilitic treatment was withheld until the course was completed. A blood Kahn test on Sept. 12 was negative. On Sept. 19 a urethral smear still showed intracellular gonococci, and there was a muco-purulent urethral discharge with hazy urine in both glasses. On dark-ground examination the sore was again positive to *T. pallidum*. It was therefore decided to start penicillin treatment for the gonorrhoea and use the opportunity offered to observe the action of this drug on the primary syphilitic lesion.

On Sept. 19, 100,000 units of penicillin were administered intramuscularly in doses of 20,000 units three-hourly. Dark-ground examination of the sore was carried out before each injection of penicillin. The following observations were made: (1) The sore was positive to *T. pallidum* before the first, second, and third injections of penicillin but was negative thereafter—that is, after 60,000 units. (2) A mild general reaction was noted and the temperature rose to 100° F. six hours after the first injection. This reaction corresponded in time to the usual Herxheimer reaction found after initial arsenic in a primary case. Twenty other patients treated with the same batch of penicillin had no reaction. (3) The next day—Sept. 20—the sore was still negative to *T. pallidum* and considerably cleaner. Urethral discharge had ceased, and urine was clear in both glasses. (4) Daily examination showed the sore to be negative to *T. pallidum* on each succeeding day until Oct. 3—i.e., 14 days after starting penicillin treatment, and at this time had almost completely healed. (Only saline dressings had been applied.) (5) The following Wassermann and Kahn results were obtained at two different laboratories:—Lab. A: Kahn test negative on Sept. 21, 24, 29, and

Oct. 5. Lab. B: W.R. double positive, Kahn positive on Sept. 26 (W.R. + + ; K.T. +); W.R. and Kahn both negative on Oct. 5.

At this stage it was considered unjustifiable to withhold routine treatment with arsenic and bismuth. This was started on Oct. 5, and it was interesting to note that after the first 0.3 g. of N.A.B. there was mild general malaise and the temperature rose to 99° F. Further treatment has been uneventful. Kahn tests on Oct. 9 and 18 were both negative.

Comment.—Although the date of exposure to infection is not absolutely definite the expectation in this case would be that blood W.R. and Kahn tests would have been positive before routine treatment was instituted. A weak positive was obtained in one laboratory, but repeated controls at this and the other laboratory were all negative. Depending on the sensitivity of the antigen, this probably indicates that the penicillin had prevented an impending positive serum reaction.

Case II

Gnr. Y. was admitted to hospital on Aug. 28, 1944, with the following history: exposure to infection two weeks and three months previously; treated for fresh gonorrhoea with 27 g. of sulphapyridine in M.I. room from Aug. 21 to 28: urethral discharge persisted.

On admission he had a purulent urethral discharge with some oedema and induration in the region of the fraenum. Clinically his latter condition was suggestive of an intra-urethral chancre. A blood Kahn test on Aug. 28 was negative. A further course of sulphapyridine was given from Sept. 2 to 6. A urethral smear on Sept. 11 and succeeding days still showed intracellular gonococci, and the urine was hazy in both glasses. Perifraenal oedema and induration persisted, but over the period Sept. 2 to 14 nine dark-ground examinations of the urethral discharge were negative to *T. pallidum* despite the clinical appearances.

In view of the sulphapyridine-resistant gonorrhoea 100,000 units of penicillin were given on Sept. 18. A urethral smear on Sept. 20 showed no gonococci, but a slight watery discharge persisted until Oct. 2. Daily dark-ground examination of this was negative to *T. pallidum*.

He was discharged from hospital on Oct. 5. There was no urethral discharge, and the urine was clear in both glasses. The oedema and induration around the fraenal region had slowly subsided after penicillin therapy and had disappeared by the time the patient left the hospital.

Comment.—Although oedema as described above is occasionally present in acute gonorrhoea it usually does not persist so long even in sulpha-resistant cases. It is felt, then, that in all probability this was a case of intra-urethral chancre despite negative dark-ground findings. In view of this and the findings in Case I it is intended to prolong the period of post-hospital surveillance in this case, regular blood tests being carried out over a period of two years.

Discussion

The present dosage of penicillin used in the treatment of resistant gonorrhoea is 100,000 units, and a group of cases was recently reported in which 60,000 units were found adequate. These dosages, then, according to the presumptive evidence of reports on the treatment of syphilis, are quite inadequate to cure this disease, but on our own observations are perfectly adequate to effect the clinical cure of a primary lesion in itself. Obviously they will also very successfully mask any primary lesion which a patient with gonorrhoea may be incubating.

The following problems now arise: (1) What interval must elapse before such an inadequately treated case will develop a positive blood W.R. or systemic manifestations of syphilis? (2) On the analogy that an early syphilis inadequately treated with the arsenicals frequently develops precocious tertiary lesions, will this also hold true of penicillin? (3) On the same analogy, is not such a patient likely to remain infective during the assumed latent period? At present we have no evidence on these points.

What, then, is to be the routine in cases of sulpha-resistant gonorrhoea treated with penicillin? We know that a certain small but definite percentage of gonorrhoea cases are incubating syphilis, which may not show until the final blood test after three months' surveillance. The reasonable assumption now is that with the advent of penicillin these cases will be completely masked, according to the observations on the two cases quoted. Two alternatives appear to be open. Either the initial dosage must be sufficient to deal with a possible coexisting syphilis (2,500,000 units) or surveillance must be extended to cover a period of (say) two years after treatment to exclude the latent systemic spread of any possible coexisting syphilis to which the patient is exposed on the present routine. In our present state of knowledge the first is obviously wasteful. The second appears to be the only fair method, not only to the patient himself but also to the community in general.

Having reviewed briefly the probable effect of penicillin in masking an early syphilis it would be well at this stage to think of the numerous patients who have had penicillin treatment for general infections. Large numbers of these have been battle casualties with heavily infected wounds. With our knowledge of conditions in the various theatres of war it is reasonable to assume that any one of these cases may have been incubating syphilis at the time penicillin treatment was instituted, and the dose, though large, may not have been the postulated curative dose. Will the patient's signs and symptoms too be masked until in a few years' time the poor unfortunate begins at an early age to suffer from anginal pain or his wife gives birth to a snuffling child?

This article is not intended to be destructive or pessimistic, however much it may appear so. Penicillin has more than proved its value as a life-saving measure and in many acute and chronic infections which previously would have led to marked general debility and prolonged hospitalization. To the venereologist it is the drug of choice in the treatment of gonorrhoea. There is no doubt that as further supplies become available it will, and must, be even more extensively used.

However, it is hoped that enough has been said here to emphasize the need for the most careful and prolonged surveillance of penicillin-treated gonorrhoea cases (and even in cases where venereal disease might be suspected in a patient treated for some other condition) until our present knowledge of the effect of the drug in syphilis is much further advanced.

Regarding the second group of cases mentioned, it cannot be too strongly advocated that, in future, routine blood tests of the whole population should be enforced by law, particularly before marriage.

Conclusion

By force of circumstances this article has been largely theoretical and referable to a very small percentage of cases. However, until we know in detail the response of early syphilis to small doses of penicillin both from the clinical point of view and from that of change in the serum reaction, the necessity for very careful assessment and prolonged surveillance of every case would appear obvious, particularly in view of the two cases described.

THE TEMPORARY CHARACTER OF "FASTNESS" OF STAPHYLOCOCCI TO PENICILLIN

BY

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It is generally assumed that micro-organisms which have been made resistant to bacteriostatic drugs or to antibiotic agents by continued subcultivation in increasing quantities of the antibacterial substance will remain "fast" after many subcultures in ordinary laboratory media. Fleming and Allison (1927) showed that *Micrococcus lysodeikticus* could be made resistant to lysozyme, and that after repeated subcultures extending over nine months in ordinary culture media this resistance was fully maintained. Similarly, bacterial resistance to sulphonamide drugs appears to be a permanent characteristic. McLeod and Daddi (1939) found that a "sulphapyridine-fast" strain of pneumococcus Type I remained resistant after 30 subcultures in broth.

Rake *et al.* (1944) subcultured pneumococcus Type III in penicillin 55 times, thereby raising the bacteriostatic dose of penicillin from 0.03 unit to 0.95 unit. After 32 subcultures of their resistant strain in ordinary blood broth the bacterio-

* Seconded for the duration of the war from the London County Council.

static dose of penicillin remained unchanged. Schmidt and Sesler (1943) made pneumococci resistant by passages through penicillin-treated mice; they then passed their resistant strain through 30 normal mice without any loss of resistance.

Spink *et al.* (1944) found that staphylococci which they had made resistant by 109 transfers in penicillin *in vitro* showed no loss of resistance after storage on veal-agar for three months in the refrigerator.

Methods

In the following experiments 100 c.cm. of broth was infected with 0.25 c.cm. of a broth culture of staphylococcus. A suitable dilution of penicillin was added to a portion of this infected broth, and a series of tubes was then set up containing the infected broth with falling dilutions of penicillin on a 20% range in a total volume of 1 c.cm. After 24 hours' incubation the last tube showing no growth was noted, and 0.25 c.cm. from the next tube, in which the staphylococci had grown out, was subcultured into 100 c.cm. of broth for the next test. This process was continued daily until the culture was highly resistant to penicillin; it was then subcultured daily in ordinary broth without any penicillin, and titrations were done at frequent intervals to determine the resistance of the strain to penicillin.

Staphylococcus Strain "Oxford H"

This is the standard strain of staphylococcus used for the assay of penicillin. Fig. 1 shows the results of subculture in

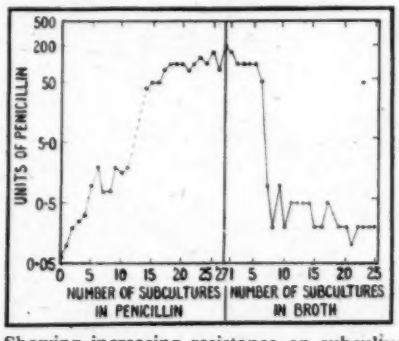

FIG. 1.—Showing increasing resistance on subculture in penicillin followed by diminishing resistance on subculture in broth. Staphylococcus "Oxford H."

penicillin and of subsequent subculture in ordinary broth. At the beginning of the experiment 0.06 unit of penicillin was sufficient to cause bacteriostasis. After 11 subcultures in penicillin 2 units were required to cause bacteriostasis. During the next two subcultures the maximum quantities of penicillin used—namely, 4 units and 10 units—failed to cause bacteriostasis, and at the fourteenth subculture 40 units of penicillin were required for bacteriostasis. After 27 subcultures the resistant staphylococci grew in 160 units but not in 200 units, and had therefore become 3,000 times more resistant to penicillin than the original culture. As noted by previous workers, the character of growth in broth and on agar had changed with increasing resistance. Growth in broth was comparatively scanty, and various colony forms were seen on solid media. Rake *et al.* found that three colony forms of their resistant strain varied in their degree of resistance to penicillin, those with the greatest morphological variation from the parent strain showing the greatest increase in resistance.

The highly resistant strain was now subcultured daily in tryptic digest broth without any penicillin, and the opacity of each subculture was noted by comparison with barium sulphate standards. During the first three subcultures the opacity was less than 1. After six subcultures, when the cocci grew in 50 units of penicillin but not in 100 units, the opacity had returned to normal, giving readings between 2 and 3, and it remained at this level until the end of the experiment. There was then a rapid fall in resistance to penicillin, and after 19 subcultures the cocci grew in 0.1 unit but not in 0.2 unit. The resistance to penicillin had therefore fallen in 19 subcultures from 3,000 times to little more than twice the original level. After 36 subcultures the bacteriostatic dose was 0.12 unit, and for the original untreated culture it was still 0.06 unit.

Slight variations in resistance to penicillin can be obtained without any exposure to penicillin. The "Oxford H" strain was found to grow in 0.05 unit of penicillin but not in 0.06 unit. It was then subcultured daily for about a month in horseflesh-infusion broth containing 2% of proteose peptone and in tryptic digest broth. The two cultures were then retested, and it was found that the infusion-broth culture still had a bacteriostatic dose of 0.06 unit, while the digest-broth culture had a bacteriostatic dose of 0.03 unit.

A resistant strain of "Oxford H" which had been subcultured 40 times in penicillin grew in 250 units but not in 300 units. After 21 subcultures in infusion broth it grew in 0.16 unit but not in 0.2 unit. When a highly resistant strain of staphylococcus "Oxford H" was subcultured on agar the fall in resistance was slower and less complete. A strain which grew in 320 units of penicillin per c.cm. but not in 400 units was subcultured daily on agar slopes. After 28 subcultures the cocci grew in 0.5 unit of penicillin per c.cm. but not in 0.6 unit.

Staphylococcus Strain "A"

Fig. 2 shows the results of a similar experiment with a different strain of staphylococcus. The original bacteriostatic dose of penicillin for this strain was 0.08 unit. After 21 subcultures in penicillin the bacteriostatic dose was 20 units, and after 10 subcultures in broth the organisms grew in 0.2 unit but not in 0.5 unit. After 36 subcultures the bacteriostatic dose was 0.2 unit, while the untreated culture

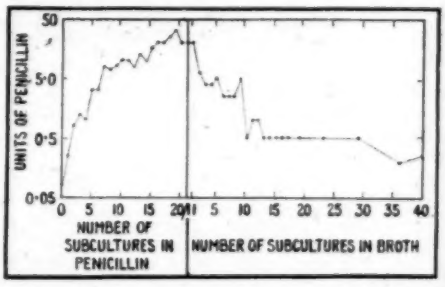

FIG. 2.—Showing increasing resistance on subculture in penicillin followed by diminishing resistance on subculture in broth. Staphylococcus strain "A."

grew in 0.06 unit but not in 0.08 unit. With this strain the bacteriostatic dose was increased 250 times by subcultivation in penicillin, and on transfer to broth it rapidly fell again to less than three times the dose required to inhibit the untreated culture. The first four subcultures in broth had an opacity of less than 1, the next four had opacities between 1 and 2, and subsequent subcultures were between 2 and 3. As in the previous experiment the cultures remained coagulase-positive throughout.

Discussion

It appears from these experiments that staphylococci which have become highly resistant to penicillin after subcultivation in increasing concentrations of the drug *in vitro* lose their resistance to such an extent on subcultivation in broth that they become sensitive to penicillin in concentrations which are easily attained in the human body. It does not seem unreasonable to suppose that staphylococci which have become resistant to penicillin *in vivo* might similarly revert to the penicillin-sensitive state on withdrawal of the drug. Indeed it seems possible that the reversion might be more rapid *in vivo* than *in vitro*, since Spink *et al.* have shown that penicillin-resistant staphylococci are much more susceptible to the bactericidal action of human blood than normal staphylococci which are sensitive to penicillin.

It seems to be a general rule that organisms which have become "fast" remain in that condition for an unlimited number of generations, and it is well known that organisms such as *Streptococcus pyogenes* and *Gonococcus* which have become resistant to the sulphonamides retain their resistance to the drug through many generations, and that cross-infections with these resistant strains breed true. Organisms other than staphylococci have not been tested in the present work, but Rake *et al.* have shown that pneumococci retain their resistance

to penicillin on subcultivation in laboratory media. It may be that penicillin-resistant staphylococci are an exception to the general rule, and that, consequently, resistant strains of this organism will not appear in clinical practice after more prolonged use of the drug.

Summary

Two strains of coagulase-positive staphylococci were made penicillin-"fast" by cultivation in increasing quantities of penicillin. They were then subcultured daily in broth without penicillin and, contrary to expectations, a rapid fall in resistance to penicillin was noted. It therefore appears that "fastness" of staphylococci to penicillin is not a permanent characteristic.

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WEIL'S DISEASE IN NORMANDY: ITS TREATMENT WITH PENICILLIN

BY

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In view of the experiences of the last war Weil's disease was not unforeseen in the present campaign in North-West Europe. Sporadic cases have occurred, and the opportunity has been seized of treating cases with penicillin. Such results as have been obtained are presented now, as no further cases have been seen for over two months.

History of Outbreak

Weil's disease is spread by infected rats who pass the spirochaetes in their urine; the organisms can live for some time in stagnant streams, in wells, and in the zoogloea-like substance on the walls of wells and sewers. It has been impossible to make detailed studies of the epidemiology of the disease, nor are these necessary. The source of the infection was almost certainly water which men used for washing. Drinking-water was supplied from water-carts or was sterilized in some way, but the supply was not sufficient for other uses; the men were forced to draw water from wells or streams for washing, shaving, and brushing their teeth. They bathed when they could in any available stream. On some sectors they lived in damp rat-infested ditches. As cases were few it was decided that the risk was worth taking, as the alternative—even if it could have been enforced—would have been that the men remained dirty or unrefreshed by bathing during the dreary and often very hot period on the Normandy beach-head.

Up to date (December, 1944) cases have been met with only in Normandy, and only from the middle of July to the end of September. It is surprising that conditions in the Low Countries have not produced further infections: there is plenty of water, both in canals and in the fields, but the weather has been unattractive for the bather, and organized bathing and ablution facilities are much better. I saw the first recognized case on July 18 with Major C. L. Davidson in a C.C.S. near Caen. The patient had had a febrile illness with severe muscle pains and a leucocytosis; on the tenth day he had a very faint icteric tint in his conjunctivae, but was convalescent. We discussed the possibility of Weil's disease, and a few days later we learnt that the agglutination test was positive. The beach-head was so small then that it was easy to tell all the physicians at C.C.S.s and hospitals to watch for it: its presence made common or garden jaundice an attractive clinical problem. Cases cropped up in many units, and when the outbreak ceased at the end of September I had been informed of 39. It is difficult to compute the extent of the outbreak; my figures must be incomplete, and cases must have been missed, especially those without jaundice. Of the 39 cases only two did not have jaundice, whereas the number should have equalled those with jaundice. I would make an informed guess that about 100 cases occurred altogether.

Some cases were very severe, and supplies of antileptospiral serum at first were scanty; it seemed possible that the leptospira might be penicillin-sensitive, and Col. J. S. K. Boyd, Deputy Director of Pathology, ascertained in a telephone conversation with the War Office that it was moderately sensitive. It was at once decided to investigate the matter. In only one case—the only fatality in the penicillin series—was antileptospiral serum given.

Clinical Features

These will not be recited at length—they are well dealt with in the standard textbooks. Those of us who were little familiar with the disease were struck by its unusual features: a brisk febrile illness with severe muscle pains as the leading symptoms, associated with a leucocytosis and complicated by signs of gross renal damage. In the presence of an outbreak this picture is highly suggestive even if jaundice does not follow. In all but two of our cases jaundice developed on or after the fifth day; in sharp contrast to "infective hepatitis," the temperature did not subside when jaundice appeared; it usually increased, and the urine still showed the signs of renal damage. In most cases there was some haemorrhagic incident—conjunctival ecchymosis, epistaxis, haemoptysis, haematemesis, purpura.

The disease if at all severe ran a longish course, the temperature was maintained for perhaps two weeks, and there were often febrile relapses later. The patients were very debilitated, but as they could not remain in the theatre of war we did not find out how long convalescence was going to take, or whether some would develop a type of cirrhosis within a few months.

Of the special types described the anginal form was rare; there were three examples of the meningeal form, but only one had an abnormal cerebrospinal fluid; lung involvement with haemoptysis, watery sputum, and abnormal signs, both physical and radiological, was not uncommon.

Laboratory Findings.—Spirochaetes were found in the blood in several cases, and in the urine in quite a number—both by dark-ground illumination. Animal inoculation was possible only when a resourceful pathologist was able to procure a guinea-pig by local purchase. In most of the cases positive agglutination tests were obtained by sending blood to the U.K. I am satisfied that the errors in diagnosis of Weil's disease have been negligible.

Penicillin Treatment

The dosage recommended was 40,000 units 3-hourly, with a total of about a million units. The average amount given was 1,125,000 units—some by continuous intramuscular drip, some by intramuscular injection—and there was a certain variation in dosage.

Our difficulties in assessing the results have been great. The disease rapidly inflicts severe damage on liver and kidneys, and to be successful any treatment must be given early enough to anticipate this; in practice this means that treatment must be started before the diagnosis has been firmly established—perhaps at a time when a diagnosis is impossible to make. We were dealing with a disease with which few of us were familiar, and no case was treated in the pre-icteric stage when there was the best chance of rapid resolution. Even if penicillin should prove to be a specific remedy it seems doubtful how often really early treatment will be practicable, unless there is so big an epidemic that everyone becomes very skilled in early diagnosis.

We have been unable to find any satisfactory measurement of progress. The numbers we had were too small to warrant any statistical approach—I have avoided any deduction from the deaths occurring in the treated and the untreated. With an elaborate laboratory service it might be possible to estimate the rate of disappearance of spirochaetes from blood or urine—this would need experimental animals, which we lacked. The most promising indication of progress was the effect of the drug on the temperature and on the number of febrile relapses. As is only too common in medicine, we were left with a clinical impression; this demands a nicety of judgment and an intellectual honesty which the observer may indeed possess but which a critic could be forgiven for doubting.

Most of the severe cases received penicillin and recovered; all observers claimed a dramatic improvement in 36 hours, which was usually reflected in the temperature chart, but with

slow improvement in jaundice and urine. Of the fatal cases, I doubt whether any treatment would have saved the two who died of suppression of urine (one treated, one not treated); the third case was not thought severe enough to need penicillin, and this patient died of auricular flutter on the 21st day: this should have been averted if there had been a specific treatment.

Lieut.-Col. L. H. Howells and Major R. R. Hughes made an intensive study of seven cases, six of which they treated with penicillin. Their conclusions were as follows:

1. Penicillin in adequate doses appeared to shorten the general effects of the disease as assessed by the duration of the fever; it had an effect on the number of febrile relapses, and these results bore a direct relation to the dosage.

2. Penicillin did not seem to influence the degree and duration of the cholaemia as estimated by the icteric index and the van den Bergh test, or to affect the rate of disappearance of icterus from the skin or of bile from the urine.

3. Penicillin did not influence the degree of nitrogen retention as estimated by the blood urea, or the degree or rate of disappearance of albuminuria.

4. Apart from the objective evidence mentioned in paragraph 1 there remains only the very definite clinical impression that cases treated with penicillin, especially with high doses, improved dramatically within 36 hours.

5. It is considered that penicillin should be given in cases of Weil's disease as soon as possible and in high doses. Once liver and kidney damage has occurred penicillin does not appear to minimize the results of this; hence it would be interesting to observe the effects of the drug during the pre-icteric phase.

Results

The results in the present series of cases of Weil's disease are as follows:

Total cases	39
Penicillin-treated	16
8 severe, 7 moderate, 1 mild. (14 confirmed by agglutination tests.) 1 died of uraemia	
Untreated	23
2 died—1 of myocarditis on 21st day, 1 of uraemia soon after admission	

Discussion

I have presented the results of the treatment with penicillin of 16 cases of Weil's disease. It would appear that there has been an effect on the speed with which the temperature falls and on the number of febrile relapses, while all the observers claimed an improvement in the patients' general condition within 36 hours. These are scanty pieces of evidence on which to base definite conclusions.

In another theatre of war penicillin treatment, in my opinion, has been considered as ineffectual, but the dosage used was inadequate—15,000 units 3-hourly. It is known that certain strains of leptospira are penicillin-sensitive *in vitro*.

In view of these facts it is felt that further work on this subject should be pursued; it is essential to give treatment early, and the dosage should be high.

I have followed this work throughout, and have seen most of the patients; nevertheless my part in this paper is that of compiler on behalf of the following physicians of 21 Army Group: Lieut.-Cols. C. L. Cope, G. G. Gillam, L. H. Howells, R. L. Mackay, I. McGolrick, I. Murray, R. E. Tunbridge—all R.A.M.C.; Lieut.-Col. J. H. Geddes, R.C.A.M.C.; and Majors H. A. Dewar, R. R. Hughes, S. B. Karani, and Capt. J. A. Lorimer—all R.A.M.C.

More than 250 hospitals in England and Wales are now using rehabilitation methods—including physiotherapy, remedial exercises, outdoor games, and handicrafts. This is nearly twice as many as a year ago, when the Ministry of Health made a special appeal to civilian hospitals to establish a rehabilitation department as soon as possible. Some hospitals are using local halls; others have been supplied by the Ministry of Health with prefabricated huts for remedial exercises and other activities. The Ministry also lends equipment for gymnastics, sports, and occupational therapy. The majority of some 400 hospitals covered by a Ministry of Health survey have appointed a member of the staff as a rehabilitation medical officer. Many of these doctors have attended special courses at selected rehabilitation centres. Other courses have been provided for physiotherapists, handicraft teachers, and others. To help with the resettlement of disabled persons in industry, large firms in the neighbourhood of certain hospitals have established special workshops in which disabled employees may be restored to working capacity by exercising the affected limbs in suitably adapted work under proper supervision.

LOCAL PENICILLIN THERAPY IN OPHTHALMIA NEONATORUM*

BY

ARNOLD SORSBY, M.D., F.R.C.S.

AND

ELIZABETH HOFFA, L.R.C.P.&S.Ed., D.C.H.

Unlike the sulphonamides, penicillin remains effective in the presence of pus. It therefore has possibilities for the local therapy of ophthalmia neonatorum as an alternative to general sulphonamide treatment of this affection. To investigate this possibility 47 infants at the Ophthalmia Neonatorum Unit at White Oak (L.C.C.) Hospital were treated with penicillin. Table I brings out the salient features in summary form.

TABLE I.—*Showing results in 47 Cases of Ophthalmia Neonatorum Treated by Various Concentrations of Penicillin. (+ = Successful Treatment; − = Failure)*

Organisms	Concentration of Penicillin: Oxford Units per c.cm.							
	500		1,000		1,500		2,500	
	+	−	+	−	+	−	+	−
Gonococci	2	2*	2	0	2	3*	5	0
Staphylococci	1	1	1	—	1	—	9	—
Diphtheroids	—	—	1	—	1	1	—	1
Staphylococci and bacilli	—	1†	—	1	1	—	3	—
Unidentified diplococci	—	—	—	—	1	—	—	—
No organisms or inclusion bodies found	—	—	—	—	—	—	2	—
Virus: assumed from the presence of inclusion bodies	—	1	—	2‡	—	—	2	—
Total	3	5	4	3	6	4	21	1

* Including one case which relapsed.
† Relapsed after clinical cure in 6 days.
‡ Both initially clear after 8 days and 4 days respectively when relapse occurred.

The Series as a Whole

(*a*) Initially, penicillin was used in a concentration of 500 Oxford units per c.cm. Eight cases received this treatment, one drop of the solution being instilled hourly during the first 24 hours, and continued two-hourly subsequently. Only three of these eight cases were cured. Two more showed an initial recovery, which, however, was not maintained. The three cured cases required treatment for 2 days, 3 days, and 6 days respectively.

(*b*) A second series of 7 cases were treated with penicillin in a concentration of 1,000 units per c.cm., the method of application in three cases being as in the first series, and in the remaining four cases the penicillin was instilled at half-hourly intervals for 24 hours and hourly subsequently. Four of this series of 7 cases showed clinical cure in 2, 4, 2, and 5 days respectively; one case did not respond to treatment, while the remaining two cases both relapsed after an initial recovery.

(*c*) A further 10 cases constituted a third series treated with penicillin, this time in a concentration of 1,500 units per c.cm. (the drops being instilled half-hourly during the first 24 hours and hourly subsequently). Six of these 10 cases showed an excellent response, clinical cure being obtained in 18 hours in one case, in 2 days in four cases, and in 3 days in the remaining case successfully treated. Two cases showed a poor response in spite of treatment for 4½ and 5 days respectively; in one case penicillin treatment was discontinued after 3 days as progress appeared inadequate; in the remaining case of this series an initially satisfactory response which gave a clinical cure within 2 days was followed by a relapse which did not respond to further penicillin therapy.

(*d*) Twenty-two infants were treated with penicillin in a concentration of 2,500 units per c.cm., the drops being instilled half-hourly for the first 3 hours, then hourly for 24 hours and two-hourly subsequently. In all but one case there was

* A report to the Penicillin Trials Committee of the Medical Research Council.

excellent clinical response, recovery in some instances being a matter of a few hours, as can be seen from the following summary:

Time taken for a Clinical Cure		Number of Cases	
3 hours	3–24 hours	1	6
7 ,,		1	
12 ,,		2	
18 ,,		1	
24 ,,		1	
27 ,,	27–43 hours	1	7
36 ,,		1	
37 ,,		1	
40 ,,		3	
43 ,,		1	
50 ,,	50–100 hours	1	7
60 ,,		1	
70 ,,		1	
78 ,,		1	
100 ,,		3	

One case is omitted from this table, as the complication of corneal ulcer—present on admission—delayed a return to normal.

One point deserves stressing. Rapidity of clinical cure does not seem to depend altogether on initial mildness of the condition. Of these 20 cases, 4 were severe; they cleared up in 36, 40, 40, and 37 hours respectively, while all the 7 cases that required 50 to 100 hours were either mild or moderate.

Differential Susceptibility of the Causal Organisms to Penicillin

Of the 25 cases in the first three series only 13 showed clinical cure, 5 more relapsed after apparent clinical cure, and 7 gave a poor response or none at all. The distribution of organisms in these different cases is summarized in Table II.

TABLE II

Organisms	Number showing		
	Clinical Cure	No Result	Relapse after Apparent Cure
Gonococci	6	3	2
Staphylococci	3	1	—
Diphtheroids	2	1	—
Staphylococci and bacilli	1	1	1
Unidentified diplococcus	1	—	—
Inclusion bodies	—	1	2

No fine conclusions can be drawn from these results. So far as this series goes it would appear that none of the organisms met in ophthalmia neonatorum are completely resistant to penicillin. A rather surprising feature emerges with the three cases of inclusion blennorrhoea present: theoretically no result would be expected, but in two cases there was an initial recovery, only to be followed by a relapse.

The 22 cases treated with penicillin in a concentration of 2,500 units per c.cm. bear out the efficacy of the drug for the variety of causal organisms of ophthalmia. As can be seen from Table I, treatment was successful in the 5 cases due to the gonococcus, the 9 caused by staphylococci, the 3 in which staphylococci and bacilli were present, and in the 2 in which inclusion bodies were found; 2 further cases in which no organisms or inclusion bodies were present also responded to penicillin treatment. No relapses were observed in this series, and the only failure was a case in which no organisms were found in the smear and the culture showed diphtheroids.

It would therefore appear that penicillin is effective over the whole range of causal organisms with the possible exception of diphtheroids—though even here two cases responded to penicillin in a concentration of 1,000 and 1,500 units respectively, and a third case showed a partial response to penicillin (1,500 units per c.cm.).

With the limited material so far investigated it is not possible to assess whether the different causal organisms respond to a varying degree to penicillin treatment. The problem is, moreover, complicated by the fact that it is not always possible to assess the significance of bacteriological findings in ophthalmia neonatorum. *Staph. albus*, diphtheroids, and some other bacilli are generally regarded as non-pathogenic. Yet it is worth noting that three of the seven cases treated with penicillin in a concentration of 2,500 units and requiring treatment for more than 50 hours showed diphtheroids—one of them in association with *Staph. albus*. In no case in which diphtheroids were found was there a rapid clinical cure. The bacteriological findings in the 7 cases requiring over 50 hours of treatment are of interest (Table III).

TABLE III

Smear	Culture	Inclusion Bodies	Duration of Treatment
Diphtheroids	Staph. aureus	Absent	100 hours
,,	,, ,,	,,	,, ,,
,,	Staph. albus	,,	50 ,,
Staphylococcus	Staph. aureus	,,	60 ,,
Negative	Negative	,,	70 ,,
,,	,,	Present	78 ,,
,,	Staph. aureus	,,	100 ,,

Cases showing diphtheroids or inclusion bodies would therefore appear to be most resistant to penicillin therapy. (*Staph. aureus*, though it appears three times in these 7 cases, is not in itself resistant to penicillin, as was evident from the excellent response in 6 other cases.)

Sulphonamide-resistant Cases

Five cases among the first 25 were treated with penicillin after a poor or protracted response to sulphonamides. Three of these were cases of gonococcal ophthalmia and responded well to penicillin, used in concentrations of 500, 1,000, and 1,500 units respectively. In the fourth case *Staph. aureus*, and in a fifth diphtheroids, were present; in both these cases there was a satisfactory response to penicillin in a concentration of 1,500 units per c.cm. Initially the first case had been treated by sulphathiazole for 12 days, and the four others by sulphamezathine for 5½, 12, 5½, and 23 days, respectively. Clinical cure by penicillin took place in 3, 4, 2, and 3 days respectively in the first four cases and in 18 hours in the fifth case.

Mode of Use

On admission the infant's eyes are irrigated with half-normal saline at room temperature and one drop of penicillin is instilled. Irrigation is also carried out before each further instillation of penicillin so long as there is any discharge. With penicillin in a concentration of 2,500 units per c.cm. irrigation is generally not necessary after 6 hours. Penicillin is continued for 48 hours after apparent clinical cure, at two-hourly intervals during the day and three-hourly at night. The drug is well tolerated by the infant's eye. Occasionally a mild transitory flushing of the conjunctiva is observed.

Comparison with General Sulphonamide Therapy

Until a standardized technique for local penicillin therapy is established no useful comparison with general sulphonamide therapy can be made. Local therapy has obvious advantages, and, moreover, avoids the danger of sensitization that the oral administration of sulphonamides carries. Frequent irrigations are, however, a trial to the infant and a considerable burden on the nurse. The present results promise to reduce these to a tolerable minimum. The dramatic results obtained by the sulphonamides are paralleled by those given by penicillin.

Summary

A total of 47 cases of ophthalmia neonatorum treated by the local application of penicillin in the form of drops is reported. Concentrations of 500, 1,000, 1,500, and 2,500 Oxford units per c.cm. were used.

An increasing proportion of satisfactory results was obtained with increase in the concentration of the drops used, the proportions in the four series being 3 out of 8, 4 out of 7, 6 out of 10, and 21 out of 22 respectively.

In adequate concentration penicillin appears to be effective against all the common causal organisms of ophthalmia neonatorum, including the virus of inclusion blennorrhoea.

It is likely that some forms of ophthalmia neonatorum respond more readily to penicillin than others. On the whole the results are of the same order as those obtained with the sulphonamides.

We are indebted to Dr. E. N. Young of the Southern Group (L.C.C.) Laboratories for her painstaking bacteriological examinations, and to the Matron and Sister Condon of White Oak Hospital for their collaboration. We are grateful to Prof. Sir Alexander Fleming for his interest and help.

PREPARATION OF PURIFIED PENICILLIN

BY

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This communication describes a simple and inexpensive method of preparing purified penicillin suitable for systemic use. The method can be carried out with the equipment available in most bacteriological laboratories. Production of penicillin in bacteriological laboratories would augment the supplies and make penicillin available to patients who otherwise could not be treated by this valuable drug.

Cultivation of the Mould

The mould *Penicillium notatum* was obtained from Sir Alexander Fleming. It was grown on a modified Czapek-Dox medium, using lactose instead of glucose (Taylor, 1943), corn-steep liquor instead of yeast extract (Clifton, 1943), and adding traces of zinc (Foster *et al.*, 1943). Yields of penicillin of 30 to 40 units per ml. were regularly obtained on this medium. The mould was grown at room temperature. The antibacterial activity was assayed by the cylinder-plate method (Heatley, 1944) and the tube-dilution method (Fleming, 1942).

Penicillin for Systemic Administration

Methods for extraction and purification of penicillin are all based on the observation that this substance can be extracted from strongly acidified aqueous solutions into ether, amyl acetate, or chloroform, and re-extracted from the organic solvent into water at *p*H 7 (Clutterbuck *et al.*, 1932; Abraham *et al.*, 1941; Meyer *et al.*, 1942). Further purification is achieved by chromatographic methods (Abraham and Chain, 1942; Catch *et al.*, 1942).

These methods proved very laborious and uneconomical, and therefore quite unsuitable for routine laboratory use. Meyer *et al.* (1942) claimed for their method a yield of over 50% of the original potency. Abraham *et al.* (1941) obtained in a form suitable for intravenous injection only about a third of the penicillin which had been present in the crude culture filtrate. The considerable losses of penicillin during purification by these methods were chiefly due to the rapid destruction of penicillin in strongly acid solutions, particularly when extraction was done at room temperature. To minimize losses, extraction had to be carried out in the ice-chest. Other features of these methods which have been found inconvenient were the large bulk of the solvents required and the long period of time (4 to 12 hours) which had to be allowed for complete separation of the amyl acetate–culture fluid mixture. Chromatographic methods for further purification of penicillin were too laborious and wasteful for routine purposes.

A search was made for a solvent which would extract penicillin from aqueous solutions at a *p*H not harmful to penicillin. It was found that most of the antibacterial substance could be extracted by n-butyl alcohol from culture filtrates adjusted to *p*H 6.4 (Berger, 1944), at which penicillin is most stable. Before extraction with butyl alcohol most of the inactive pigments and other impurities could be removed from the culture fluid by precipitation with ammonium sulphate. The salting out of impurities with ammonium sulphate did not result in any loss of antibacterial potency of the filtrate, and incidentally caused still more complete extraction of penicillin by butyl alcohol. Further experiments have shown that the solubility of penicillin in butyl alcohol is considerably greater than in the culture fluid at *p*H 6.4, thus allowing extraction with relatively small amounts of solvent. Penicillin dissolved in butyl alcohol was quite stable. Two samples of sodium penicillin obtained from the same butyl alcohol extract—one immediately after extraction and the other after having been kept in butyl alcohol for 48 hours in the ice-chest—contained the same amount of penicillin. The butyl alcohol–culture fluid mixture separated well, separation being complete after 10 to 15 minutes.

Penicillin was precipitated from butyl alcohol by light petroleum ether and obtained as an aqueous solution of the sodium salt by addition of a suitable quantity of sodium bicarbonate solution. During this procedure further purification of penicillin was achieved as certain impurities were left behind in the organic solvents. At this stage a fifteenfold to fortyfold concentration of penicillin could be obtained, and although extraction was carried out at room temperature the losses of penicillin were never greater than 15%, and were as a rule as small as 5%, of the amount present in the culture fluid.

Penicillin solutions were further purified by extraction into chloroform at *p*H 3.6 in the presence of ammonium sulphate (Meyer *et al.*, 1942). The addition of sodium bicarbonate solution to the chloroform extract again yielded an aqueous solution of sodium penicillin. The losses during this stage of purification were small, and usually less than 5% when the penicillin solution was well chilled before acidification. A further tenfold concentration was achieved by the chloroform extraction, and solutions of sodium penicillin containing 3,000 to 4,500 units per ml. were finally obtained.

Technical Details

The technical details of the method were as follows: The culture fluid was adjusted with 20% phosphoric acid to *p*H 6.4 The Lovibond comparator, with bromothymol blue as indicator, was used for this purpose. The culture fluid was then cooled in the ice-chest and 40% of ammonium sulphate was dissolved in it. The precipitate which formed was filtered off in the ice-chest through a Chardin filter paper. Five volumes of the filtrate were then extracted by shaking in a separating-funnel with one volume of butyl alcohol, and after separation the extracted culture fluid was discarded. To the butyl alcohol extract were then added an equal volume of light petroleum ether and one-eighth of the total volume of the mixture of 2% sodium bicarbonate solution. The butyl alcohol–petroleum ether mixture was extracted for a second time with a fresh portion of the 2% sodium bicarbonate solution.

The first extract of sodium penicillin, after having been chilled to approximately 4° C., was adjusted to *p*H 3.6 with 20% phosphoric acid, using the capillator method with bromophenol blue as indicator. Again 40% of ammonium sulphate was dissolved in the acidified penicillin solution, which was then extracted with an equal volume of chloroform. After separation penicillin was extracted into sodium bicarbonate solution by shaking ten volumes of the chloroform extract with one volume of 2% sodium bicarbonate solution. The chloroform was then extracted for a second and third time with fresh portions of sodium bicarbonate solution. The accompanying table gives the results obtained in a typical experiment.

Table showing Results obtained with the Butyl Alcohol Extraction Method followed by Further Purification and Concentration of the First Extract by the Chloroform Method

No.	Sample	Units per ml.	Volume of Fluid in ml.	Total Units	Percentage of Units Recovered
1	Culture fluid	31·6	14,000	442,400	—
2	1st extract from butyl alcohol	384·5	980	376,810	85·1
3	2nd extract from butyl alcohol	55·0	850	46,750	10·5
4	Extracted culture fluid	0·5	14,000	7,000	—
5	1st extract from chloroform made from No. 2	3,156·6	100	315,660	83·7
6	2nd extract from chloroform made from No. 2	489·7	100	48,970	12·9
7	3rd extract from chloroform made from No. 2	40·7	100	4,070	1·0
8	No. 2, after chloroform extraction	3·5	980	3,430	—

The aqueous solutions of penicillin were then adjusted to approximately *p*H 6.6 with dilute phosphoric acid. When kept in the ice-chest they retained their full potency for at least two months. The penicillin solutions were sterilized by passing through a Seitz filter; they were then stored in sealed ampoules and used for systemic treatment of patients. These chloroform-free penicillin solutions retained their full antibacterial potency at 4° C. for at least a further six weeks. The penicillin solutions could be freeze-dried without difficulty.

Second extracts from the butyl alcohol and the second and third extracts from chloroform were further purified and concentrated by the chloroform method to give a product assaying 250 to 500 units per ml. These solutions were incorporated into creams or used as drops for treatment of infections of the eye.

Before dispensing, the penicillin solutions were tested for sterility. Suitable amounts of penicillase, prepared according to Harper's (1943) method, were added to 1-ml. quantities of the penicillin solution and incubated aerobically and anaerobically in heart broth for three days. The penicillin solutions appeared to be non-toxic

Rabbits injected intravenously with 20 ml. of a solution containing 60,000 units of sodium penicillin did not show any immediate or delayed reactions. Intracutaneous injections into the abdominal wall of rabbits and guinea-pigs did not cause any local inflammatory reactions, and the cutaneous swelling arising from the injection rapidly disappeared.

Morgan *et al.* (1944) when administering penicillin intravenously by the continuous-drip method noticed the development of thrombosis or thrombophlebitis in a large proportion of their cases. In view of these experiences intravenous application was not tried; the intramuscular route was employed exclusively. Usually 4 to 6 ml. of the penicillin solution (about 12,000 to 18,000 units) was injected every three hours. The continuous-intramuscular-drip method was also used in suitable cases, giving 80,000 to 100,000 units in 24 hours. Up to the present more than 40 patients suffering from various diseases due to penicillin-sensitive organisms were successfully treated in this way. Details of the clinical results will be published later. The injections of penicillin did not cause any immediate or delayed painful sensations, and no irritative or inflammatory reactions were observed.

Penicillin was also repeatedly injected intrathecally in two cases of pneumococcal meningitis and one case of streptococcal meningitis. The injections were therapeutically effective, were well tolerated, and did not cause any untoward symptoms.

Penicillin for Local Treatment

Crude culture filtrates containing as little as 2 to 10 units of penicillin per ml. have been used successfully by Pulvertaft (1943), Alston (1944), and Hobson (1944) for treatment of many localized infections. The clinical use of crude culture filtrates appears inadvisable and potentially dangerous for two reasons. First, such filtrates always contain large amounts of protein, which is also produced by the mould and secreted into the culture fluid. The repeated application of such fluids to large raw surfaces is likely to lead to sensitization—a point also made by Raper and Coghill (1943) in connexion with "home-made" penicillin. Secondly, culture filtrates from media which do not contain yeast extract or corn-steep liquor may contain notatin (Kocholaty, 1942; Coulthard *et al.*, 1942; Roberts *et al.*, 1943), a potent antibacterial substance of extreme toxicity.

Clutterbuck *et al.* (1932) found that by adjusting the fluid to *p*H 3.6 most of the protein and a considerable proportion of pigment could be flocculated and filtered off from the culture fluid without loss of penicillin. This method has been successfully employed for this purpose, and incidentally the gummy substances formed from the corn-steep liquor during autoclaving were precipitated out at the same time. Kocholaty (1943) found that notatin is not formed in cultures of *P. notatum* which contain corn-steep liquor.

The protein-free penicillin solutions were not toxic. Two rabbits, weighing about 1,600 g. each, were injected with 50 ml. intravenously in 10-ml. portions in the course of two days. The animals did not show any immediate or delayed reactions of any kind. The protein-free penicillin solutions have been used successfully in the treatment of extensive infected burns, wounds, abscesses, ulcers, discharging sinuses, throat and ear infections, empyemata, and gonococcal vulvovaginitis, and in selected cases of osteomyelitis and compound fractures. The penicillin solutions proved non-irritating and did not cause untoward symptoms in any case. Manifestations of allergy were not observed even when application of penicillin was continued for a month or longer.

Summary

A simple and efficient method of preparing purified penicillin for systemic treatment is described.

Intramuscular injections of penicillin solutions obtained with this method were therapeutically effective, were painless, and did not cause untoward effects of any kind.

This work has been done under the direction of Prof. P. L. Sutherland, to whom I am indebted for many valuable suggestions and for help and advice throughout the course of the investigation. Thanks are due to Sir Alexander Fleming for a subculture of the mould; to Dr. J. W. Trevan, of the Wellcome Research Laboratories, for a sample of standardized penicillin; and to Dr. D. Engel, medical superintendent of Staincliffe County Hospital, Dewsbury, for clinical application of the penicillin. Acknowledgments are also due to Mrs. B. Berger, Mr. G. Denton, and Mr. H. Schofield for technical assistance.

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THYROID HYPERPLASIA AFTER PROLONGED EXCESSIVE DOSAGE WITH THIOURACIL

BY

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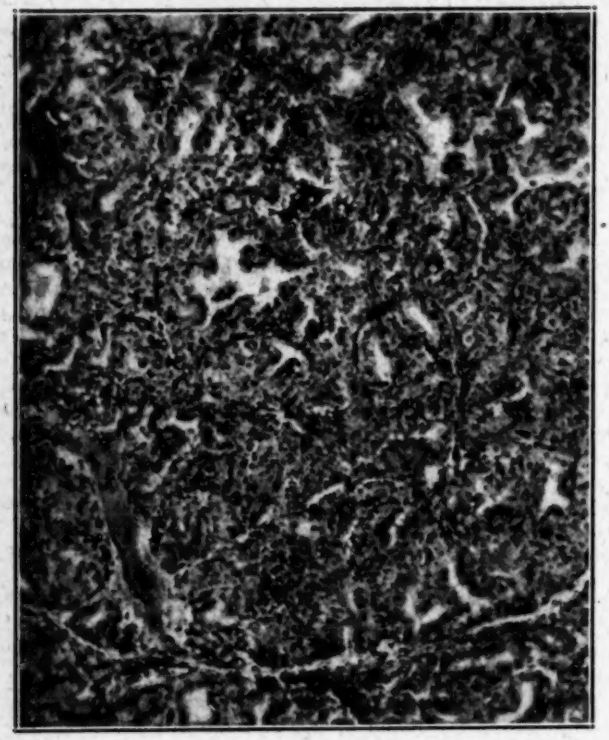
During the past year we have treated with thiouracil a total of 31 patients suffering from thyrotoxicosis. The results obtained are very similar to those noted by other workers. They are on the whole most encouraging, and comparable to those produced by successful thyroidectomy. Only one of the patients developed serious toxic reactions to the drug, consisting of leucopenia and signs of acute sensitivity. Another appeared relatively drug-resistant, and, in spite of prolonged treatment, thyrotoxic symptoms and signs persisted. With the exception of the case noted below no significant changes in the size of the goitres occurred as the result of treatment, though they usually became softer, and a transient slight increase in size was often noted at the menstrual period. It seems to be the general experience of other workers that thiouracil in therapeutic doses does not as a rule affect the size of the goitre significantly, but Himsworth (1944) has reported three cases in which the goitre increased considerably in size as the result of treatment with thiouracil—an effect which he attributes to overdosage.

There seems to be general agreement that the optimum dosage during the initial period of treatment should be 0.6 g. daily. This dosage should be kept up for from three to four weeks, at which time a fall in the basal metabolic rate has usually become significant. No increased effect is obtained by doubling the dose, as any additional quantity appears to be immediately excreted in the urine. There is as yet no definite consensus of opinion as to the dose required for maintenance treatment. There can be little doubt that 0.2 g. daily is adequate. We have never noticed any evidence of "escape" from the control of the drug when a reduction in the dosage has been made from 0.6 to 0.2 g. daily. There is no definite evidence, however, that 0.2 g. is the minimum dose required. We have latterly treated a number of patients with a maintenance dose of 0.1 g. daily, and it is our impression that this dose is quite sufficient. One case, through a misunderstanding, received an excessively large maintenance dose for a period of five and a half months.

Case Record

A female patient, aged 33, suffering from classical thyrotoxicosis, had experienced her first symptoms one year before admission to hospital. A small primary goitre was present. She was treated

with 0.6 g. of thiouracil daily for 20 days, and was then given a maintenance dose of 0.2 g. daily for a week. She was discharged from hospital feeling very well. Her weight had increased by half a stone in a month, and her B.M.R. had fallen from + 55 to + 8. A mild tachycardia was the only residual sign of her thyrotoxicosis. She was told to continue to take 0.2 g. of thiouracil daily, but owing to a misunderstanding she actually took 0.4 g. As her home was in the far North of Scotland it was impossible for her to report to us regularly, and she was seen once a month by her own doctor. The first three reports from him were most satisfactory, but the fourth stated that she was not quite so well, though no specific symptom was noted beyond some lack of energy. By the fifth month this symptom had become pronounced, and a swelling of the neck was reported. The patient was immediately sent for, and on readmission, five and a half months after her discharge, was found to have a very large soft goitre. This was associated with a mild degree of myxoedema. Her weight had increased by one stone since discharge from hospital, her B.M.R. had fallen to −20, and her blood cholesterol had risen from 220 to 266 mg. per 100 c.cm. Her white blood count of 5,600 showed no significant alteration. Thiouracil was immediately stopped, and in two weeks' time she felt considerably better, her B.M.R. having risen from −20 to −3. No change had occurred, however, in the size or consistency of the goitre, and thyroidectomy was undertaken, principally for cosmetic reasons. At operation the thyroid was obviously enlarged, and was firm though not hard. The cut surface was typical of the hypertrophy associated with a primary toxic goitre which had not been treated by iodine. A section of the gland is shown in the accompanying photomicrograph. It can be seen that



there is extreme parenchymatous hyperplasia and an almost complete absence of colloid, the picture being similar to that produced by Mackenzie in animals treated with goitrogenic substances. After the operation the patient made an uninterrupted recovery, and was discharged home feeling well.

Comment

It is thought worth while to record this case as providing another instance to those noted by Himsworth of thiouracil causing a great enlargement of the goitre in a previously thyrotoxic patient. It gives practical proof of the theoretical assumption that if the pituitary is stimulated to produce excess thyrotrophic hormone by overdosage with thiouracil an increase in the size of the goitre will occur similar to the hyperplasia of the thyroid produced in experimental animals by thiourea and its derivatives, and by sulphaguanidine. A rapid and significant enlargement of the goitre in a patient under treatment with thiouracil may thus be evidence of overdosage.

REFERENCE

Himsworth, H. P. (1944) *Proc. roy. Soc. Med.*, **37**, 693.

Medical Memoranda

A Method of Administering Systemic Penicillin

Owing to the shortage of rubber tubing systemic penicillin is being administered by 3-hourly intramuscular injections, and it has been found that a good many patients complain of the pain and discomfort, and "come to dread the needle." The following method has been adopted and found satisfactory.

Pressure-tubing, outside diameter 1/4 in., length 3/4 in., is worked over the intramuscular needle and a glass cap applied to seal off (Fig. 1). The intramuscular needle is fixed in a suitable site with elastoplast strapping. Another strip of elastoplast is applied over the first, the projecting rubber tubing with glass cap is wrapped in sterile gauze, and the elastoplast is fixed in place. 15,000 units of penicillin in 1.5 c.cm. are drawn up into an all-glass syringe, and the needle removed. The nozzle of the syringe is inserted into the rubber tubing, which is steadied by forceps, injection given, and a sterile glass cap applied. Sterile gauze is wrapped round and elastoplast is reapplied (Fig. 2). The intramuscular needle can remain in place for four days without changing to a new site.

FIG. 1

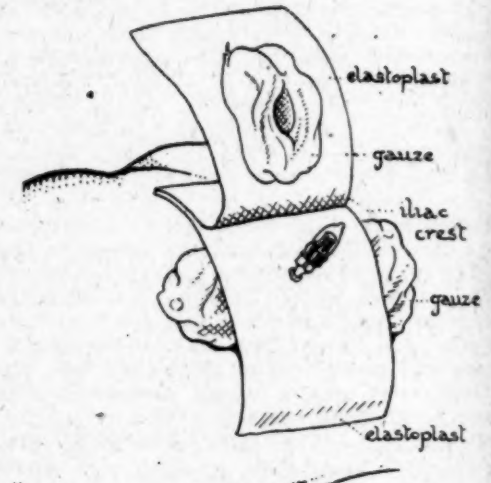


FIG. 2

I wish to thank Mrs. W. K. Somerton for the illustrations, Mr. Garner of the pathological department for the suggestion of the glass cap, and Dr Shepherd, the medical superintendent, for permission to publish.

Barnsley Hall Emergency Hospital. H. L. MILLES, M.R.C.P.

A Case of Meningococcal Meningitis Treated with Penicillin

Since little is at present known about the effect of penicillin in meningococcal infections this case is considered worth recording.

CASE RECORD

A male child aged 18 months was admitted with a four-days history of repeated vomiting after all feeds. Previously he had been quite well. On the day before admission his mother had noticed that he felt hot and had a rash on his chest. There was no urinary retention and the bowels were normal. He had had gastro-enteritis at 2 months and at 6 months of age. The gain in weight had been good. On examination the child looked ill, being pale and lethargic. The anterior fontanelle was closed. There was slight diminution of skin elasticity. Some fading petechiae could just be seen on the thorax. The posterior cervical muscles were rigid, opisthotonos was

present, and a positive Kernig's sign and Brudzinski's neck sign were found. The C.N.S. showed normal cranial nerves and reflexes apart from absent abdominals. No abnormality was detected clinically in the chest, cardiovascular system, abdomen, throat, or eardrums, and the urine was normal.

Lumbar puncture on admission revealed a turbid C.S.F. under pressure: cells, 600 per c.mm., of which 66% were polymorphs; protein, 100 mg. per 100 c.cm.—globulin test positive; sugar, present but reduced; chlorides, 680 mg. per 100 c.cm. Microscopy showed numerous extra- and intra-cellular diplococci. Culture yielded a pure growth of *N. meningitidis* which proved sensitive to penicillin and sulphonamides. A blood count done at the same time showed R.B.C. 4,650,000 per c.mm., Hb 12.5 g.%, W.B.C. 16,200 per c.mm., of which polymorphonuclear cells comprised 59%, lymphocytes 29%, and monocytes 12%.

Shortly after being admitted the child had a convulsion and was comatose. As an alternative to intramuscular sulphonamide a request was made for penicillin. This was supplied and an intramuscular drip set up containing 67,500 units in 16 fl. oz. of 0.9% saline. The temperature was then 101.5°, pulse 122. Overnight the temperature rose to 103°. Owing to poor absorption only 23,000 units were given in the first 24 hours after the drip was started. During the second period of 24 hours 112,000 units were given, made up in 0.45% saline, about 8 fl. oz. being used. The patient was now taking fluids by mouth. At this time the urine contained acetone and reduced Benedict's reagent fully.

Seventy-two hours after the start of penicillin administration (202,500 units absorbed) the rectal temperature was 99.5° and the child had so much improved that he recognized his parents and took hold of toys offered to him. Neck rigidity, though still present, was less marked. A second lumbar puncture showed a clear specimen, with cells 120 per c.mm. and chlorides 735 mg. per 100 c.cm. Culture yielded no organism, and the C.S.F. inhibited growth of the standard Oxford strain of staphylococcus.

Sulphamezathine was now given orally (0.5 g., 6-hourly), but ten hours later the temperature rose to 104°. A further course of penicillin was then started, 202,500 units being given during the next three days. By this time the temperature had fallen to 99° (rectal) and the child was able to walk about his cot, appearing normal in every way. He has since made an uneventful recovery. Total penicillin, 405,000 units in 6 days.

COMMENT

While under normal circumstances penicillin given intramuscularly does not enter the C.S.F., the observations in this case suggest that in the abnormal conditions of meningitis it may do so. It is evident that the dose given in the first 24 hours was inadequate. Penicillin should have been continued after 72 hours without a pause.

The continuous intramuscular drip was employed for the following reasons: (1) steady maintenance of blood level; (2) little disturbance of patient—0.1% novocain was included in the drip; (3) more numerous sites available. The daily dose was made up every 24 hours. A fresh drip apparatus was used each day, the whole being assembled complete with needle and then sterilized immediately before use. The outer sides of the left and right thighs were used alternately, the skin being cleansed with 2% C.T.A.B. and flavine in spirit.

I am indebted to Dr. Stanley Wyard, senior physician, and to Dr. Richard Hollick, R.M.O., for permission to publish this case.

GEORGE H. TEE, M.R.C.S., L.R.C.P.,
House-physician, Victoria Hospital for Children, Chelsea.

A Case of Weil's Disease Treated with Penicillin

The following record of a case of Weil's disease has two points of interest. The first is the clearing of the leptospira from the urine after only 6 injections of penicillin, coincident with rapid clinical improvement; the second, the demonstration of leptospira in the blood and urine on the day that the agglutination titre was as high as 1 in 1600.

CASE HISTORY

A private soldier aged 38 was invalided from France with pyrexia of six days' duration and reached this hospital on the evening of Sept. 12, 1944.

The patient reported sick on Sept. 7, complaining of a severe frontal headache and a sensation of chilliness and shivering. His temperature was 102.8° F. Next day he complained of generalized aching and soreness of the eyes. His conjunctivae were injected and his temperature was now 103° F. His liver was palpable and tender, and he vomited continuously. His blood was negative for malaria parasites and *Leptospira icterohaemorrhagiae*. There was a mild leucocytosis of 12,800. He was evacuated by air on Sept. 11, and the last entry on his medical card stated that his general condition was poor.

Clinical examination on arrival at the hospital showed that he was now lightly jaundiced and his conjunctivae were heavily injected. He stated that during August he had bathed frequently in a rat-infested river. On the 13th, examination of his urine revealed the presence of large numbers of spirochaetes morphologically identical with *L. icterohaemorrhagiae*. Blood was taken for the agglutination test and a few drops were examined by dark-ground illumination. Surprisingly, leptospira similar to those in the urine were easily found. Later the report from Prof. Gardiner, of Oxford, stated that the serum was positive for agglutination of *L. icterohaemorrhagiae* to a titre of 1 in 1600.

Penicillin therapy was started at 6 p.m. The dosage was 20,000 units intramuscularly three-hourly until Sept. 17 and then four-hourly until it was stopped on the 20th. The total dosage was 900,000 units. Before the penicillin was begun the patient complained of a marked degree of general malaise. The following morning he said he felt all right and thought himself fit enough to get up. However, his temperature did not become normal until the 16th. Leptospira could not be demonstrated in his urine or blood from 9 a.m. on the 14th onwards. Specimens of his urine were examined daily until the 30th, and in none of them was the organism discovered. The patient did not develop any after-fever, and was discharged perfectly well on Sept. 30.

A. E. CARRAGHER, M.B., D.P.H.,
Assistant Lecturer in Pathology, Welsh School of Medicine, and Pathologist to Llandough Hospital.

Internal Hydrocephalus complicating Pneumococcal Meningitis Treated with Penicillin after Sulphonamides

Internal hydrocephalus is a well-known complication of post-basic meningococcal meningitis, but the following case shows that when the clinical course of the disease has been considerably prolonged by therapeutic measures it can arise also in infections due to the pneumococcus.

CASE REPORT

A male infant aged 2 months was admitted to hospital, having been unwell for a few hours, during which he had one convulsion. On examination he was found to be extremely ill, vomiting brown material, and grossly dehydrated. His temperature was 100.6° F., pulse uncountable, and respiration rate 40 a minute. No clinical signs were found in his chest or the central nervous system, but the C.S.F. was turbid and contained Gram-positive diplococci. On culture a pneumococcus was isolated which proved lethal to mice.

Subcutaneous saline was administered and 0.5 g. of sulphapyridine by mouth every four hours, but after 5.5 g. had been given this was stopped on account of persistent vomiting. This treatment was accompanied by a fall in the temperature to 97° F., but next day, the fourth after admission, it rose to 101.4°. Sulphathiazole was then administered in the same dosage, but starting with 1 g. The temperature did not settle and the infant remained very ill. On the seventh day 10,000 units of penicillin were injected into the right lateral ventricle, after which 2,000 units were given intramuscularly every four hours. By the ninth day the C.S.F. contained only a few cocci; these were avirulent to mice. On the next day the temperature became steady at a normal level. The child's general improvement was pronounced, and no more organisms were recovered from the C.S.F. On the seventeenth day he became unwell again, and developed attacks of twitching with cyanosis and some vomiting. No C.S.F. could be obtained from the spinal canal in the lumbar region, but that in the basal cisterns was under raised pressure. It contained 600 mg. of protein per 100 c.cm. and 60 lymphocytes per c.mm.; no organisms were seen in it, and cultures were sterile. The child died two days later, on the twentieth day after admission, the illness having lasted for 21 days altogether.

Findings at Necropsy.—Nothing abnormal was found outside the central nervous system. The brain was fixed by withdrawing fluid from the cisterns and ventricles and replacing it with formalin 24 hours before opening the skull. Films of this fluid showed effete polymorphs, some of which contained degenerate-looking Gram-positive cocci. Cultures of the C.S.F. were again sterile. Many adhesions were present between the pachy- and lepto-meninges, and a dense fibrinous exudate surrounded the brain stem and filled the cisterns. All the cerebral ventricles were markedly dilated down to and including the fourth. They all contained turbid fluid and fibrin coagula. In histological sections of the meninges the exudate was seen to contain many polymorphs. The choroid plexus was covered with a similar exudate, but this contained many Gram-positive cocci as well.

DISCUSSION

Death was caused by internal hydrocephalus due to the fibrinous exudate. In their series of 16 cases of pneumococcal meningitis treated with penicillin Cairns, Duthie, Lewin, and Smith (1944) had one case of obstruction of the aqueduct of Sylvius, but this was apparently due to pressure of an abscess. Evans (1944) saw no such condition in his small series of cases of purulent meningitis. The likelihood of the development of such a fibrinous exudate in the early stages of the infection would seem to be another reason for treating all cases of pneumococcal meningitis with penicillin as early as possible—a procedure already recommended by Cairns *et al.* in their paper.

I have to thank my colleague Dr. P. Forgacs, under whose care the child was, for his co-operation.

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Cairns, H., Duthie, E. S., Lewin, W. S., and Smith, H. V. (1944). *Lancet*, 1, 655.
Evans, A. L. (1944). *J. Amer. med. Ass.*, 124, 641.

Treatment of Ulcers by Plaster Casts

The Meru district of Kenya is inhabited by about 120,000 Africans and is heavily infected with yaws. The standard of living is very poor, and food shortages periodically lead to outbreaks of ulcers, some of which approximate to a nutritional type; others are simply yaws, and no doubt many are of mixed type. In the comments that follow no endeavour is made to distinguish the types, as all are equally intractable in certain cases and all react equally well to plaster-of-Paris treatment.

Late in 1943 several bad ulcer cases were admitted about the same time. One was so severe that amputation seemed the likely solution. All meant dressings, which were a misery to the nurses, the patients, and the wash-boys who had to deal with piles of filthy dressings. They were also a heavy expense, as doubtless many of the worst dressings were thrown away surreptitiously by the wash-boys. All these patients were getting N.A.B. and bismuth, a diet sufficient to increase the weight in the other patients, tonics, and treatment for worms if required. Locally, we rang the changes on eusol, hot foments, dry dressings, hydrarg. perchlor., cod-liver-oil ointment, elastoplast, copper sulphate, and carbolic (which usually required morphine preparation). There was no specific, and some patients treated earlier in the year had long spells in hospital.

Then we tried plaster-of-Paris casts (P.P.) and the whole situation changed. Six of the worst cases were scraped or encased without scraping, and their reactions were watched carefully. The pain eased within two days, and the temperature dropped within about five days; but the most noticeable thing was the mental change—from despair to cheerfulness and joking. This treatment has not failed, in any of some 40 cases, to lead to the casting off of sloughs, formation of healthy granulations, and proliferation of skin. The following are brief notes of 5 typical cases.

Case Histories

Case 1.—Chuka female aged 35, admitted Nov. 4, 1943. Large ulcer 7 in. in length, extending almost right round the leg, leaving a strip of healthy skin 2 in. wide over peronei. Greenish base, with sloughing muscles. Offensive smell and very painful. Warned probably need amputation unless case reacted unexpectedly well. On Nov. 10, under ethyl chloride general anaesthesia, the sore was scraped, powdered with sulphanilamide, covered with lint on which zipp had been smeared, and encased in P.P. Two days later she had no pain; her temperature was lower, though the pulse continued at 120. Her general condition showed rapid improvement; her face filled out, and on Nov. 19, impelled by curiosity, we removed the cast. Almost the whole area was covered with healthy granulations. There was no smell, and no sloughs were present except one small tag, which was cut off. New P.P. was applied: 17 days later, when this was removed, the whole area was healthy and new skin had proliferated for half an inch all round. She could walk with a slight limp. Next day she was skin-grafted with Thiersch grafts, and mosquito netting was superimposed. Hot foments were applied. After a little delay owing to blebs forming under the new skin, she walked off home, healed, 6 weeks from application of the first P.P.

Case 2.—Meru male aged 1. Big toe amputated by ulcerative process. Head of metatarsal exposed. Smelly, with oedematous undermined edges. One month's duration. Dressings applied for 14 days. Some improvement, but still very unhealthy. P.P. applied, and patient discharged. Returned in 14 days. The mother said the child was happy and had had no pain. On removal the sore was reduced from 1½ in. diameter to half that size. Healthy granulation over metatarsal. Sent out with dressings.

Case 3.—Meru male aged 20. Shallow ulcers round toes. Feet very sweaty. Treated with salicylic spirit, as considered possibly fungous. No improvement after 15 days. P.P. applied. Patient sent out. On return in a fortnight was soundly healed. No return in 3 months.

Case 4.—Meru male aged 23. Admitted Nov. 19, 1943. Ulcer 8-shaped, the centre being over the head of the second metatarsal; 5 in. in length—half on dorsum and half on sole; second toe gone. Foul and very painful. Edges raised and indurated. Swelling had caused big and third toes to be separated by 2 in., which area was occupied by the ulcer. On Nov. 20, without scraping, zipp and P.P. applied up to above the ankle. Much oozing necessitated more P.P. being added. A good patient, he waited for a month. On removal of plaster only a small linear sore remained—1½ in. by 1/2 in. He left rejoicing.

Case 5.—Embu female aged 10. Ulcers of toes and nail-beds extending on to dorsa and soles; raised oedematous edges and purulent bases; 9 months. Pain severe; much weeping over dressings. On Nov. 2, 1943, nails avulsed and ulcers scraped: no improvement. On Nov. 10 zipp and P.P. At once the whole picture changed. The patient had no further pain, and when the P.P. was removed on Nov. 29 most of the ulcer was healed and there were healthy granulations over the rest. The nail-beds were healthy. (This is an important point, as nail-bed infections usually prove most intractable.)

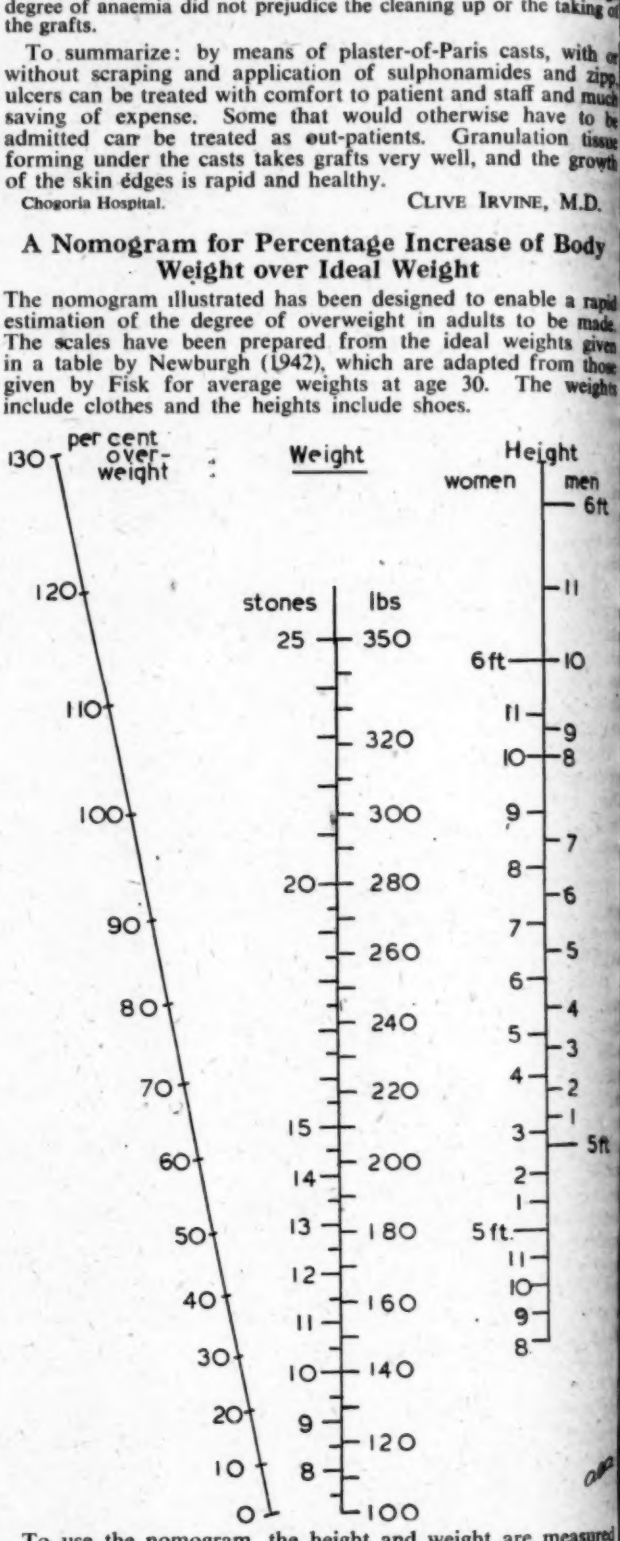
Other cases successfully treated include a leper with a linear crack across the sole, at the base of which the os calcis was exposed. Nothing had availed to heal till P.P. was tried. Case 10 in my series, which it would take up too much space to give in full, was similar to Case 1, except that she continued to have pain and a temperature—forcing us to take down the P.P. at weekly intervals. The result, however, was the same, and after 14 days' P.P. she was ready for grafting. At the moment of writing, on the 20th day, grafts have taken well and she is having treatment for foot-drop due to the position of the foot at rest while in her village. A high degree of anaemia did not prejudice the cleaning up or the taking of the grafts.

To summarize: by means of plaster-of-Paris casts, with or without scraping and application of sulphonamides and zipp, ulcers can be treated with comfort to patient and staff and much saving of expense. Some that would otherwise have to be admitted can be treated as out-patients. Granulation tissue forming under the casts takes grafts very well, and the growth of the skin edges is rapid and healthy.

Chogoria Hospital. CLIVE IRVINE, M.D.

A Nomogram for Percentage Increase of Body Weight over Ideal Weight

The nomogram illustrated has been designed to enable a rapid estimation of the degree of overweight in adults to be made. The scales have been prepared from the ideal weights given in a table by Newburgh (1942), which are adapted from those given by Fisk for average weights at age 30. The weights include clothes and the heights include shoes.



To use the nomogram, the height and weight are measured and a straight line joining the points on the height and weight scales is produced to cut the percentage scale. The point of intersection gives the percentage over ideal weight. If the zero point on the percentage scale is joined to the appropriate point on the height scale, the intersection on the weight scale gives the ideal weight.

A. B. ANDERSON, B.Sc., Ph.D., M.R.C.S.

REFERENCE

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Reviews

FACIAL RECONSTRUCTION

Traumatic Injuries of Facial Bones. By John B. Erich, M.S., D.D.S., M.D., Consultant in Laryngology, Oral and Plastic Surgery, Mayo Clinic, and Louie T. Austin, D.D.S., F.A.C.D., Head of Section on Dental Surgery, Mayo Clinic, in collaboration with Bureau of Medicine and Surgery, U.S. Navy. (Pp. 600; illustrated. 36s.) Philadelphia and London: W. B. Saunders Company.

Reconstructive Surgery of the Eyelids. By Wendell L. Hughes, M.D., F.A.C.S. (Pp. 160; illustrated. 21s.) London: Henry Kimpton.

Traumatic Injuries of Facial Bones is businesslike and useful. The book is set out in the form of an atlas, with photographs of patients, radiographs, or models on one side of the page, and full and detailed instructions for treatment on the other. Thus every possible variety of mandibular fracture is represented (mostly in the form of plaster reconstructions), and the reader can quickly learn the appropriate treatment for each. The authors seem to prefer arch wires to cap splints for most of their cases. Direct skeletal fixation is used when the fragments cannot be controlled without it. The different varieties of maxillary fractures are next described. Here again arch wires are prominent, with fixation to a head-cap, either directly or indirectly. Malar and nasal fractures are treated on lines similar to those employed in this country, except that internal splints are used inside the nose without anxiety. Multiple facial fractures receive careful consideration, and their repair is gone into in great detail.

A considerable section of the book is devoted to bone-grafting of the mandible, for which solid pieces of iliac bone are used, and a further section to restoration of facial contour, both by inlay grafting and by cartilage transplants. The final section describes the application of a plaster head-cap, the insertion of skeletal pins, the details of wiring in all forms, and the construction of metal splints.

The book is well printed on good-quality paper (rare in home productions), and the 333 illustrations could not be bettered. There can hardly be a problem in injury of the facial bones for which an answer cannot be found quickly and easily in this manual. It is a first-class presentation of the subject.

The monograph *Reconstructive Surgery of the Eyelids* was prepared as a thesis and is largely concerned with the repair of eyelids after partial or complete removal for neoplasm, and as such is a useful addition to a library.

The major part of the book is taken up with the historical development of plastic procedures, illustrated in the main from the original papers. Unfortunately the illustrations have suffered by reduction and overcrowding, and it is not only difficult to make them out but also difficult to correlate the text, the illustration, and the legend thereof. Nor is the text improved by overburdening with names and reference numbers. Innumerable procedures are sketchily described, without any attempt at critical appraisal, which is of little value to the student. Thus, for example: "Judging by reports in the literature . . . in attempting to reconstruct a fornix, if some living tissue is wrapped around the form it suffices whether it be a mucous membrane or skin from the same individual, mucous membrane from another individual of the same species, fetal membrane, or even conjunctiva from a foreign source, such as a rabbit." Would that it were so simple!

In the latter part of the book Dr. Hughes describes some of his successful cases of replacement of complete lid losses, chiefly from the opposing lid and adjoining cheek tissues. This section is well worthy of study, though to-day one would have preferred additional information on wartime injuries. One cannot help admiring the energy of the author in regimenting 451 references.

MENTAL ABNORMALITY AND CRIME

Mental Abnormality and Crime. Introductory Essays. By R. N. Craig, W. N. East, R. D. Gillespie, E. Glover, D. K. Henderson, E. O. Lewis, D. R. MacCalman, A. MacNiven, E. Miller, J. D. W. Pearce, J. R. Rees, G. de M. Rudolf, G. M. Scott. (Pp. 316. 18s.) London: Macmillan and Co. 1944.

Studies in crime must always be of interest to the medical profession, since more and more is crime being recognized as an individual disability, and more and more are social problems becoming linked with those of health. Of the papers so far published in the series *English Studies in Criminal Science* this is the most interesting to doctors in general, apart from those engaged in psychiatry. The thirteen essays which this book contains cover nearly all of the psychiatric aspects of criminology. One of particular interest is that by Dr. MacNiven, in which the question of responsibility is discussed, especially in relation to the M'Naghten rules. It is clear that partial responsibility will have to be more generally recognized, and indeterminate sentences for purposes of treatment be more often inflicted. Dr. Gillespie deals informatively with the connexions between the psychoneuroses and crime, and postulates that if crime is to rank as psychoneurotic there must be no real gain to the criminal, or the apparent gain must be shown not to be the real meaning of the act for the individual. The crime must be shown to be the outcome of conflict, and the criminal behaviour to be a substitute for or a compromise between the opposing tendencies. The criminal should be demonstrated to present other signs of psychoneuroses.

Dr. MacCalman's essay on traumatic neurosis in relation to compensation also merits study. As he points out, a single shock is seldom the sole cause of a breakdown, though it may precipitate this from a psychoneurotic background. Similarly neither work nor settlement in a lump sum is a panacea, for anxiety about capacity to work and financial security prolongs the illness. Early and complete psychological treatment is required, and without it results are likely to be poor. The section on juvenile delinquency is unimpressive, and gives a poor idea of all that is being done and all that has been found out in this branch of criminology. This is somewhat mitigated by an excellent report by Dr. Glover on the origins, methods of work, and results of the Institute for the Scientific Treatment of Delinquency. Altogether this interesting collection will well repay careful study.

TWO BOOKS ON NURSING

The Practice of Nursing. By Hilda M. Gration, S.R.N., S.C.M., D.N. (Pp. 420; illustrated. 12s. 6d.) London: Faber and Faber.

Clinical Procedures and their Background for Senior Nursing Students. By Agnes E. Pavey, S.R.N., D.N. (Pp. 331; illustrated. 8s. 6d.) London: Faber and Faber.

There are so many good textbooks on nursing that new additions not only must reach a high degree of perfection in detail but must preferably make some new method of approach. On the latter count Miss Hilda Gration's book on *The Practice of Nursing* certainly presents a more humane attitude than some books on this subject—when tested on such matters as the hour of waking, bed-making, and cups of tea! But there are errors in detail that impair its value. As early as page 15 a picture of a clinical thermometer upside down gives an uneasy feeling, aggravated by the spelling "albumen" on page 56 (for albumin in the urine), and "pulmonary tuberculosis" would have been better than "phthisis" on page 63. (The word "tuberculosis" does not even appear in the index.) The same old-fashioned terminology is perpetuated on page 156 with the use of "scruple," excluded from the *British Pharmacopoeia* many years ago. More serious faults are to be found. For example, the details of taking blood for a Wassermann test do not make it clear that the needle must be sterile, nor do they indicate the importance of rinsing with normal saline so as to avoid possible haemolysis. Another omission is that it is not made clear that all liquid milk is potentially dangerous; pasteurization is not mentioned, although as a concession milk is directed to be boiled for ill babies and for the newborn. It is a pity that a close study has revealed such faults, for the author has an attractive style and the illustrations are of good quality and well chosen.

Miss Agnes Pavey's book is open to similar fault-finding on grounds of accuracy and terminology. An appendix on "diseases, syndromes, and symptoms known by proper names" contains many "howlers." But a more serious criticism can be made: there is far too much here on details of diagnosis. Tests for liver efficiency and kidney function seem matters which should be outside even the senior nurse's curriculum, and surely the nurse does not need to know details of staining for the tubercle bacillus.

Notes on Books

A fourth edition has reached this country of *Public Health in South Africa*, by Prof. E. H. CLUVER, director of the South African Institute for Medical Research. Like its predecessors, this edition is addressed mainly to students of medicine, and the author has succeeded in his aim of presenting information in simple terms and in a concise form It will also prove useful to the large body of workers all over the Union of South Africa who, in addition to medical officers, are concerned with the protection and promotion of public health. The descriptions of various public health services assume that the pre-war arrangements will continue; but, as the author says in his preface, no one can predict with any degree of accuracy what the medical organization will be after the war. The publishers are the Central News Agency, Ltd., Johannesburg.

The second of the two reports containing selected documents from the proceedings of the council of U.N.R.R.A. at its meeting at Montreal last September has now been published (H.M. Stationery Office; 1s.). Readers who are interested to know how supplies for immediate relief in liberated countries were estimated will find some account of it and of the creation of "stockpiles" of food in the statements of Lieut.-Gen. G. N. McCready and of the representative of the Combined Food Board. Difficulties and problems encountered in Italy, especially Naples, are described, and the publication also contains the text of the council's resolutions.

Preparations and Appliances

INSTRUMENT FOR CONTINUOUS AND ACCURATE ADMINISTRATION OF PENICILLIN INTRAMUSCULARLY

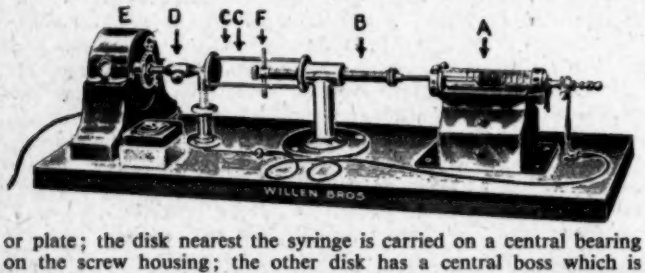
Dr. C. E. LAST, medical officer, Queen Mary's Hospital for Children (L.C.C.), Carshalton (evacuated to Dryburn Emergency Hospital, Durham), writes:

The difficulty of giving penicillin by continuous intramuscular drip is recognized by many; the difficulty being one of controlling and accurately regulating the amount of fluid given to such proportions as will be continuous and, at the same time, not cause too much pain and discomfort, nor waterlogging of the tissues.

The usual drip apparatus which is controlled by clamping a rubber tube, either with or without the assistance of capillary glass tubing, is quite efficient for intravenous injections or for intramuscular injections over short periods at rates which exceed 1 or 2 minims a minute. But these amounts are gross, and when continued for several days cause pain and waterlogging with periodic and capricious interruption of the flow—and one of the essential features of successful penicillin administration is that it shall be continuous at the prescribed amount and that absorption shall not be interrupted. But materially to reduce these amounts in bulk and to keep the flow both accurate and continuous require endless supervision, day and night. This constant supervision is always exasperating and often fruitless; it disturbs the patient's rest and absorbs an enormous amount of time.

Description of Apparatus

A very simple instrument has been designed and made to meet all these difficulties. A is a Record syringe which rests in a trough and is held by a suitable clip. B is a 3/8-in.-screw with 16 threads to the inch passing through a metal housing supported on a pillar. CC are two parallel arms fixed at each of their ends in a brass disk



or plate; the disk nearest the syringe is carried on a central bearing on the screw housing; the other disk has a central boss which is coupled to the spindle of the hour hand of a clock or small electric motor. D is a small clutch, controlled by a finger screw, which intervenes between the boss and the spindle. F is a detachable pin which transfixes the main screw and is held in position by a small finger screw. E is a clock or motor electrically driven. All the parts are aligned and mounted on a board.

The clock spindle or electric motor makes one complete revolution every hour and turns the parallel arms with it. The arms engage the pin which turns the screw, and, as the screw proceeds, the pin slides along the arms. The screw has 16 threads to the inch and therefore takes 16 hours to travel one inch; in 24 hours it travels 1½ in., pushing the piston of the syringe as it goes. The travel of 1½ in. of the piston of a 10-c.cm. syringe represents a trifle less than 8 c.cm. Therefore there is a continuous and positive delivery at the nozzle of the syringe of fluid at the rate of, say, 8 c.cm. in 24 hours, or 1 c.cm. during every 3 hours. In minims this works out at 1 minim every 10 minutes 17 seconds, delivered punctually and without fail, no more and no less. A 20-c.cm. syringe would deliver about 13½ c.cm. in 24 hours, or, say, 1 minim during every 5 minutes 25 seconds.

Method of Use

100,000 to 120,000 units of penicillin are dissolved in 8 c.cm. or 14 c.cm. as the case may be, and it is led through Southey's tubing and passes intramuscularly by means of a hypodermic needle, with or without additional side holes—the instrument being placed on a table 12 to 18 in. above the level of the patient. The connexions between the syringe and the tubing and the needle and the tubing are Record metal ends.

When a 24-hour run has been completed the finger screw controlling the clutch is loosened and the screw B run back by hand; the syringe is refilled, or, better still, a fresh syringe with a fresh charge is taken, the exposed metal ends are flamed and reconnected, the moving parts repositioned, and another 24-hour run is started. Assembly, filling, and refilling only take a few moments; the syringe can be renewed without disturbing the needle and tubing, and a needle can be changed without disturbing the syringe and tubing.

Advantages and Precautions

Pain and inconvenience to the patient are practically absent, his sleep is not disturbed; and, as the small amount of penicillin delivered is absorbed as fast as it arrives, there is no waterlogging. The considerable amount of time spent by the nursing staff in observations and adjustment is saved.

Children are easily dealt with. One little child aged 2 years with osteomyelitis of the femur and sinuses was put in a double plaster spica and a 16-days treatment of 100,000 units a day was carried out through a gap in the plaster over the only thigh available without any distress or evidence of complaint. A 10-c.cm. syringe was used and the needle changed 6 times.

Under normal running conditions there is no "seeping" behind the piston, owing to the fact that there is a negative pressure in the syringe and tubing system. Seeping can only occur when an internal resistance is built up which more than neutralizes the negative pressure, that is equivalent to 12 to 18 in. of water. Needle block is the main cause of this. Therefore seeping is to be regarded as the warning that the needle requires changing. However, with the concentrations used, needle block has so far not occurred under 24 hours; 36 hours is a critical time, but there have been many uninterrupted runs of 48 hours and a few of 3 days, when the needle is changed as a routine. Some authorities advocate a change of needle every day and, with all discomfort reduced to a minimum, this could not be a hardship to the patient. In addition to the evidence of "seep," a small glass pressure gauge is positioned in the tubing system, which reveals very early any needle block; this gauge also has a "boost," which frequently enables an early blocking to be cleared.

The original experimental instrument was run off the back of a standard alarum clock and has been in continuous use at the Dryburn Emergency Hospital for the past 10 weeks. I also have in use at the same hospital an instrument electrically driven and similar in appearance to the one pictured here.

I am greatly indebted to Willen Bros. Ltd., of 44, New Cavendish Street, London, W.1, for the trouble they have taken in manufacturing the instrument as illustrated, and for having made the various changes and modifications that tests showed to be necessary. The final working drawings have been placed solely in their hands to produce the instrument in accordance with the authorized design.

TYROTHRICIN

"Tyrothricin" is the new name given to the antibacterial substance extracted from cultures of *B. brevis*, as originally demonstrated by Dubos. It is separable into two constituents—gramicidin (the name originally given to the whole extract), which is highly active against Gram-positive bacteria only, and tyrocidine, which is more toxic but acts also on some Gram-negative species. Tyrothricin is unsuitable for the systemic treatment of bacterial infections, but is a very powerful antiseptic when applied locally, and has been used successfully for treating wounds, infections of the conjunctiva and cornea and of the ear, nose, and throat; there are also favourable reports on its use in empyema and certain skin diseases. Tyrothricin has now been put on the market in England by Sharp and Dohme Ltd. (Mulford Biological Laboratories, Hoddesdon, Herts), who also publish a valuable booklet describing the history of its development and indications for its use, with a useful bibliography.

Tyrothricin concentrate (human) Mulford is supplied in 1-c.cm. and 20-c.cm. vials of a solution containing 25 mg. per c.cm.; this is diluted fiftyfold or more in sterile distilled water for use.

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THE NATURE OF PENICILLIN ACTION

It has been generally accepted until recently that penicillin is bacteriostatic rather than bactericidal. This has doubtless been a good thing, since it has encouraged attempts to maintain continuous action for a long period; only in these circumstances will any antiseptic substance, whatever the nature of its action, help to eliminate bacteria from infected tissues. But in recent months several workers in this country, notably J. W. Bigger,[1] have obtained evidence that penicillin, so far from merely restraining the growth of bacteria, actually kills them. These observations have been prompted by a natural curiosity about the mechanism by which penicillin achieves its effect. We are no longer content with the knowledge that a certain substance under given conditions will kill a particular micro-organism: we want to know by what chemical process this is brought about, and such knowledge has been obtained for a large variety of chemotherapeutic agents within the past few years. Not only does it place treatment on a fully rational instead of a semi-empirical basis, but it may point the way to the synthesis of related agents with extended powers.

There are several facts of which any explanation must take account. One is the peculiar specificity of the action of penicillin. Everyone knows that some bacteria are susceptible and others not, and that Gram-staining reaction does not without exception distinguish them; what is not so generally recognized is that the degree of susceptibility is so variable. Some species commonly classed as totally resistant are in fact affected by higher concentrations; they include even the typhoid bacillus and salmonellas, and it was predicted several years ago by the Oxford workers[2] that the treatment even of these infections may prove worth while when pure penicillin is freely available. Other bacteria which most people dismiss from their minds where penicillin is concerned appear in a new light in view of the observations of H. F. Helmholz and C. Sung[3] on the action of penicillin on bacteria in urine. No one has thought of treating with penicillin any urinary tract infections except those due to staphylococci, but these authors have shown that a concentration 90 times greater than the minimum necessary for *Staph. aureus* has the same effect on *Str. faecalis*, while a 240-fold increase will bring in *Proteus*, and a 900-fold some strains of *Bact. coli*; only *Bact. aerogenes* and *Ps. pyocyanea* were unaffected at this and even a higher level. Owing to the very high concentrations attained in the urine by systemic administration two at least of these relatively resistant organisms may succumb to treatment in this special situation only. These examples illustrate the enormous range of susceptibility of different bacteria; the peculiarity in their constitution which accounts for this has yet to be discovered. Another fact of observation is the penicillin-induced change in morphology first observed by A. D. Gardner.[4] Cocci swell to thrice their normal size, and bacilli elongate themselves into monstrous threads; this change naturally gave birth to the idea that penicillin prevents bacterial division. A third noteworthy fact is the immense possible range of habituation to penicillin, at least in some species. Whatever the action of penicillin, it is one which the bacterial cell can learn to counter or circumvent; the studies of E. W. Todd and others, which are described on page 111 of this issue, show that *Staph. aureus* can be trained to withstand a concentration 3,000 times greater than the maximum tolerated by the original culture. Unlike the pneumococcus, which has been shown to retain this property in subsequent culture or mouse passage, this organism lost it rapidly in normal media. It is consoling to read that similar treatment applied to the gonococcus failed to induce any appreciable increase in resistance.[5]

A helpful method in determining the nature of chemotherapeutic effect is to identify substances which neutralize it; this was the path which led to success in the study of sulphonamide action. So far no application of this method to the study of penicillin has been discovered; one secret of its therapeutic success is the fact that penicillin acts equally well in any medium not actually destructive to it, including any body fluid, pus not excepted. Whether the substance recently extracted by W. M. M. Kirby[6] from penicillin-resistant staphylococci will be of any interest in this connexion remains to be seen; it is not penicillinase; and, indeed, the evidence seems clear that when normally susceptible bacteria acquire resistance to penicillin this change is not due to acquisition of the power to make this substance, nor do all naturally resistant species form it. Another possible line of approach is to study the influence on penicillin action of simple physical factors such as concentration and temperature, with a view at least to discovering whether their effects on penicillin and on ordinary disinfectants are the same. Such a study is described by L. P. Garrod in the opening paper of this issue, and appears to have brought to light one peculiar feature—namely, that increase in concentration above what by clinical standards is a very moderate level brings no added effect, and will indeed, if carried far enough with impure penicillin such as is now being used, actually diminish the rate of disinfection. Subject to the results of further studies, which will evidently be dependable only if conducted with pure material, it seems that within very wide limits the action of penicillin is indifferent to concentration; its full effect is exerted at a certain quite low level—probably well under 1 unit per ml.—and no addition to this will alter the result. This property, should it be verified, is peculiar and may well be significant. It has a distinct bearing on practical treatment and indicates a policy by which efficiency and economy can be combined.

Laboratory findings have also been translated into therapeutic policy of quite a different kind by Bigger,[7] whose argument rests on the observation that in a population of

[1] *Lancet*, 1944, **2**, 497.
[2] Abraham *et al.*; ibid., 1941, **2**, 177.
[3] *Amer. J. Dis. Child.*, 1944, **68**, 236.
[4] *Nature*, 1940, **146**, 837.
[5] A. W. Frisch, *Amer. J. Syph.*, 1944, **28**, 627.
[6] *Science*, 1944, June 2, p. 452.
[7] Loc. cit., and *Irish J. med. Sci.*, 1944, **553**, 585.

staphylococci, of which the vast majority are killed by penicillin overnight, a few survive even for days. Linking this with the hypothesis that penicillin kills only dividing cells, he attributes this survival to the existence of a few cells in a dormant condition; these "persisters" are assumed to be the agency by which infection is kept alive when penicillin treatment fails in such a condition as osteomyelitis. Since "persisters," when they multiply, give rise to cells which are normally susceptible to penicillin, a therapeutic method akin to tyndallization (intermittent sterilization) is proposed; treatment is to be interrupted in order to permit bacterial growth and thus restore vulnerability. Whatever its other merits, this hypothesis stands or falls according to whether it is true that penicillin acts exclusively on multiplying bacteria. Garrod has examined this question, and contends that neither the influence of temperature nor the death rate in cultures of different ages can be interpreted in support of Bigger's hypothesis. On the other hand there is evidence that the presence of a bacteriostatic agent such as sulphathiazole will interfere to some extent with the action of penicillin. Lest too high a significance should be attached to observations of this kind, it must be remembered that reproductive activity affects the susceptibility of the bacterial cell to other disinfectants for which no such special type of action has ever been assumed, and we do not know whether combination with a bacteriostatic agent would affect them similarly. Perhaps the weightiest argument against adopting the policy of intermittent administration is to be found in clinical experience. In an analysis of causes of failure in penicillin treatment, A. L. Bloomfield, W. M. M. Kirby, and C. D. Armstrong[8] rank the too-early interruption of treatment as a major factor in their unsuccessful cases. Many others have insisted that the attack on infection by penicillin must be relentless and long-continued. He must be a bold man, not to say a rash one, who will deliberately reverse this policy.

NEGLECTED CHILDREN

The new social services to be provided after the war are designed to shower benefits upon the citizen while requiring from him hardly any co-operation beyond the payment of contributions. The encouragement of initiative and enterprise in the individual is not a popular policy. Dr. A. E. Martin, assistant medical officer of Leicestershire, who won the Haldane prize and medal in 1943 with an essay on child neglect,[9] points out the melancholy fact that many families have such grave inherent defects that, no matter what the State may do, their members cannot utilize State-provided opportunities. The problem of child neglect has itself been largely neglected by local authorities, though their existing social and health services cover every house and family in their districts. The success of any scheme for controlling and preventing it must depend first upon an efficient system of finding the neglected children and keeping them under observation. At present the health service, which supervises the child until 5, and the education committee, which is responsible for him after that, often work fairly closely together. Almost every case of neglect should be detected by one of them, but the difficulty is that the various officers have been faced with apparently insoluble problems. The work is so sordid and depressing that, as no definite scheme exists for calling in help, many children have not had efficient treatment. As a first essential, according to Dr. Martin, there should be some person on the central staff of the health authority to whom all cases may be reported, who is available for advice, and who can give some of his time to the scheme. Normally he would be one of the medical officers. He would be the pivot of the whole scheme. Thus a teacher who suspected that a child in the school was not properly cared for would report it as he now reports a child with defective sight. The administrative medical officer would call for a report on the home conditions from the school nurse or health visitor. This would stimulate her to pay detailed attention to the case, and a series of home visits might bring the parent up to the mark. In a more severe case medical inspection could be arranged; the sanitary inspector might be asked to help on the housing or sanitary side; a medical officer's visit to the home might have a good influence, and, where all else failed, the National Society for the Prevention of Cruelty to Children might be called in.

The larger part of child neglect is due to a dull or feeble mind in one or both parents. This sets an arduous and never-ending task to the health visitor, who must use the highest qualities of patience, tact, and persistence in educating the mother in household routine, cleaning children, washing clothes, and the rest of the household duties. When this work is properly done improvement is almost invariable. Health visitors are too highly qualified to be allowed to give much of their time to each family, and more social workers will have to be provided. For parents who wilfully or thoughtlessly neglect their children the inspector of the N.S.P.C.C. must be called into collaboration. Some authorities are reluctant to do this for fear of destroying the confidential relationship between the health services and the mothers of the district. Much experience shows, however, that full co-operation and interchange of information can exist without damaging the confidence of the parents. Prosecution is of little use unless the child has to be removed completely from the parents' care. The society is better qualified than the local authority to prosecute, and the combination of evidence by its inspector and a doctor or nurse of the local authority would form the most helpful basis for most cases.

The law is at present far from satisfactory, and in the present state of public opinion it would be very hard to draft a Bill which would give adequate control over neglected children and at the same time safeguard the rights of parents. The only certain method of getting children removed is to produce evidence of really bad conditions at the last visit, but this course can be adopted only after very careful thought. The most important necessary reform, according to Dr. Martin, is some scheme to bridge the gap between the voluntary supervision of the society and the cases where children must be completely removed. A neglected child should be

[8] *J. Amer. med. Ass.*, 1944, **126**, 685.
[9] *Public Administration*, Summer, 1944.

taken away, not because the parent has been convicted but because its own neglect and suffering have been proved. The local authority should be obliged to look after children removed for neglect, and such children should not have to be sent to an approved school. Concerted propaganda addressed to medical officers, directors of education and their staffs, magistrates, and the general public would be vital. Such a scheme, Dr. Martin says, could be inaugurated by circulars from the Ministry of Health and the Board of Education. Interest in it could be sustained by annual summaries prepared by the medical officers and published in their annual reports. Dr. Martin undoubtedly exposes a serious gap in our present social services which will have to be closed, at any rate in part, if the new provisions are to bear fruit, and wholly if we are to have a sound and healthy population in the years to come.

THE HEALTH OF LONDON

The interim report for 1943 of the County Medical Officer of Health for London[1] comes to hand almost twelve months after the year to which it relates—a circumstance which robs its statistics of some of their interest, especially as 1943 was a relatively uneventful year for London compared with the years preceding and following. It will be noted that the infant mortality was a fraction higher, and the maternal mortality a fraction lower, than in 1942, and that among infectious diseases cerebrospinal fever continued to decline; diphtheria had only one-quarter of its pre-war incidence; dysentery increased, though enteric fever, a disease spread mainly by the same channels, was almost negligible; scarlet fever was more prevalent than in recent years, and of somewhat heightened virulence; and measles at one point threatened to assume epidemic proportions. Notifications of tuberculosis increased, though the number of deaths remained about the same. The only epidemic disease which caused real anxiety was influenza. Here the number of admissions to the L.C.C. hospitals rose steeply at the end of the year, and recollections of the devastating epidemic of 1918–19 were stirred; but by the end of January, 1944, the incidence had fallen to the seasonal normal.

The school medical service returns show that the condition of London children in the third and fourth years of war was in some respects better than in the pre-war year of 1938. The proportion of children in whom an unsatisfactory state of nutrition was found in 1938 was 6.6%, and this had been reduced in 1942 to 6.2%, and in 1943 to 6%. The proportion of children with defective vision and of those with adenoids and enlarged tonsils declined notably, and the only outstanding increase was in the number of children found with obvious decay of the teeth. It should be added that the children inspected by dental surgeons are spread over all ages, and are not confined, as are the medical inspection returns, to the four routine age groups. The number of children examined, on which the percentages are based, was little more than half in the recent years what it was in 1938. An interesting comparison is given in the report concerning the trend of infant mortality in London and in New York during the present century. The New York figures have always been better than those of London. In 1900 the infant mortality in New York was 135 per 1,000 births, and in London 159, and the figures in 1943 were 30.2 and 50.7 respectively. The decrease in the deaths of infants, especially since 1935, has been more pronounced in New York than in London—a fact not wholly explained by war conditions in the latter city, and calling for further investigation. From a list of causes of infant deaths it appears that there has been a much greater reduction in mortality from gastro-enteritis and respiratory diseases in New York than in London during the last forty years, and especially during the last decade, and the death rate from miscellaneous causes, but particularly infective and parasitic diseases, injury at birth, and lack of care of the newborn, is more than twice as high in London.

The history of the last war has been repeated in the continued fall in the number of mental patients in L.C.C. institutions. An attempt has been made at St. Ebba's Hospital to assess the value of electric convulsion therapy and insulin therapy given to patients. Of the first 100 female depressive patients who were treated with electric convulsion therapy 87 were cured of their depression, of whom 74 were discharged; the other 13 had for various reasons to be detained; 13 of the discharged patients relapsed and had to be given further treatment. Of 72 female acute schizophrenics who were given electric convulsion therapy and insulin, treatment had been completed in 64 cases at the time of the review, and of these 64, 56 had recovered sufficiently to return home. Similar results were obtained in certain groups of male patients.

The year 1943 saw the introduction by the Council of miniature mass radiography, the unit beginning its operations at St. Luke's Hospital, Chelsea. Up to the time of the report 13,334 miniature films had been taken, and among these 433 revealed some significant abnormality requiring large films to be taken. Of the large films 110 showed pulmonary lesions calling for investigation, 30 showed cardiovascular lesions needing investigation, 155 showed calcified and other lesions in which further investigations were not necessary, and 94 showed no abnormality. The examinees have been factory and office employees, civil defence personnel, and children in secondary schools in the neighbourhood of the hospital. In all cases in which evidence of disease was found the patient's doctor was communicated with, and the *x*-ray film and report were forwarded to him.

[1] Published by the London County Council, price 6d., post free 7d.

HEALTH RESEARCH IN INDUSTRY

In the early days of the last war munition workers laboured very long hours in an effort to make good a shortage of shells, but their output fell and sickness and fatigue increased. This failure to meet the needs of a modern army at war led to the appointment of the Health of Munitions Workers Committee, who were to advise the Government on matters affecting the health and efficiency of those in munition factories. This was the first attempt in this country to investigate scientifically and comprehensively the effects of conditions of work on health. This Committee was succeeded by the Industrial Fatigue Board (later the Industrial Health Research Board of the Medical Research Council), which, by its terms of reference, had opportunity to study all classes of industrial work. But with the return of peace and unemployment the Board had little encouragement from industry. Nevertheless, it survived the rigid economies of 1924, to flourish once again with the revived stimulus of war.

The story of the Board's present activities is told in a report issued this week of the proceedings of a conference held last September.[1] In 1942 the Medical Research Council reconstituted the Board and gave it new terms of

[1] *Health Research in Industry*. Industrial Health Research Board, M.R.C. H.M.S.O., 1945. (6d.)

reference, to include the whole subject of industrial medicine and disease. In May, 1943, the M.R.C. set up a new Department for Research in Industrial Medicine at the London Hospital, and under Dr. Donald Hunter its staff are energetically investigating both the old and the new toxicological hazards with which industry has to contend. But these are problems confined to specific industries. It is therefore encouraging to know that the combined efforts of this new department and others at the London Hospital are being given to a study of the widespread problem of rehabilitation and resettlement. At Cambridge the M.R.C. has established a Unit of Applied Psychology, where more fundamental research is being done on fitting the man to the job and the job to the man. Besides these two units there remain those carrying out equally important but less dramatic investigation into sickness incidence, methods of dust sampling, and the many problems associated with the heating, ventilation, and lighting of workplaces.

Industrial health research must be closely linked with other types of medical and sociological study directed to the health and welfare of the man at home as well as at his job. It must link up, too, with management, the worker, and Government Departments concerned with the health of those in factories, mines, transport services, and offices. There must be facilities for determining the toxicity of various compounds before they are used in production. A wider view of the problem of the worker and his environment should bring together research workers, town planners, and industrialists to prevent the increasing loss of greensward, and the pollution of land, water, and air with industrial effluents. "It is not necessary for the physical appearance of industry to be that of an abomination standing where it should not." A move in the right direction is being made. Departments of Industrial Health have been established at three universities in industrial cities, and close contact between these and other departments of the university, local industries and medical practitioners, the M.R.C.'s Industrial Health Research Board, and the Factory Department of the Ministry of Labour will yield handsome dividends of knowledge. Sir Edward Mellanby has said: "Research can only be a spearhead, and a spearhead without a shaft and without somebody to hurl it is no good whatever." The shafts are the industrial medical officers and technicians. But the whole weapon can be hurled with effect only by an enlightened industrial community.

ASSISTANTS AND LOCUMTENENTS UNDER THE "PAY-AS-YOU-EARN" SYSTEM

It has for many years been the accepted practice of the Inland Revenue Department to regard locumtenents as exercising their profession in a particular way, and not as "employed" by the doctor in whose practices they worked from time to time. The result was that they were regarded as assessable to income tax under the rules of Schedule D and not of Schedule E, and that result was not only convenient to both the parties concerned but was more equitable inasmuch as it gave the locumtenent the normal Schedule D basis on which to claim professional expenses (including agency fees, travelling costs, etc.), of which he would have been unfairly deprived if he had been held to the very strict and limited basis applicable under Schedule E. The introduction of the "pay-as-you-earn" system led apparently to some misunderstanding of the view taken by the Revenue, and in order to clarify the position the matter was raised with that Department by the Northern Branch of the British Medical Bureau. In a letter dated Nov. 27, 1944, the Inland Revenue have stated their view as follows:

"With reference to your letter of Nov. 3 and the previous correspondence I am to say that a doctor who takes a series of engagements in each of which he acts as a deputy for a doctor practising on his own account is, in the view of this Department, assessable under Case II of Schedule D of the Income Tax Act, 1918. If it is established that he is so assessable any short-term appointment which he may take—for example, a substitute for an absent assistant or in a hospital—will be included in the Schedule D assessment, and no question of deduction of tax under pay-as-you-earn will arise.

"A doctor who is employed as assistant is, however, in the view of this Department assessable under Schedule E, even though he may change his job frequently.

"Tax should therefore, as a general rule, be deducted under the pay-as-you-earn system from payments made by a doctor to an assistant, whatever the length of his engagement. Tax should not, however, be deducted from payments made to a locum unless he produces a Form P45 showing the payments made to him and the tax deducted therefrom in previous weeks of the year."

It is understood from the last paragraph that it is always incumbent upon the principal to deduct tax under P.A.Y.E. where he engages a doctor as assistant; but, where the principal engages a doctor to act as his deputy, the principal is not required to deduct tax unless the locumtenent produces a Form P45. The statement as a whole appears to be clear and satisfactory, but there are one or two points to which it may be desirable to refer. In the first place the line of distinction between locumtenent and assistant may not always be clear. For example, an individual engaged as a locumtenent may stay on assisting in the practice, even becoming eventually a partner in the firm. Clearly all such cases must be dealt with on their own facts and preferably in consultation with the Inspector of Taxes. Secondly, there may be a little practical difficulty where a doctor ordinarily working as a locumtenent takes temporary duty as an assistant to, rather than as the deputy of, the local practitioner. What should the latter do in such circumstances? His appropriate action will depend on the manner in which the locumtenent's (i.e., in the hypothetical case his "assistant's") income-tax affairs are dealt with—and that is a matter outside his knowledge. The most effective means of overcoming such a difficulty seems to be for the locumtenent to notify his own Inspector of Taxes on the infrequent occasions when he is on the point of acting as an "assistant," requesting him to authorize his "employer" *not* to apply the "pay-as-you-earn" procedure in his case. Lastly, errors and oversights are apt to occur in any arrangement into which the human element enters. What should be done if in fact tax is deducted from the fees or salary in such circumstances that a refund by the "employer" is impracticable? We presume that on the Inspector of Taxes being informed of the facts it would be arranged that credit would be given against the tax payable on the locumtenent's Schedule D assessment for the amount by deduction from him under "pay-as-you-earn," or alternatively that the latter amount would be repaid by the Revenue as having been deducted unnecessarily.

We much regret to announce that Sir Henry Gauvain, M.Ch., F.R.C.S., medical superintendent of Lord Mayo's Treloar Cripples' Hospital and College, Alton and Hayling Island, since its foundation in 1908, died on Jan. 19.

Major-General Sir Ernest Cowell, C.B., D.S.O., has just been appointed Principal Medical Officer to the Health Section of the Control Commission for Germany (British Elements).

Reports of Societies

NUTRITIONAL ROLE OF MICROFLORA IN THE INTESTINES

A conference of the Nutrition Society was held on Dec. 30 at the London School of Hygiene and Tropical Medicine, Dr. W. R. WOOLDRIDGE presiding, to discuss the nutritional role of the microflora in the alimentary tract.

The papers at the morning session were mainly concerned with the nutrition of ruminants. Dr. A. C. THAYSEN suggested that the value of the bacteria present in the rumen should be ascribed not only to their ability to break down cellulose but to the nutrients derived from the digestion of the bacteria themselves after their passage from the rumen into other regions of the intestines. Mr. FRANK BAKER, describing technique for the study of the bacterial population of the rumen, said that in his view pure cultural methods gave an inadequate picture, and direct microscopical observation of the micro-organisms present in their natural habitat was necessary. Dr. J. A. B. SMITH discussed the formation of protein from non-protein sources of nitrogen, such as urea or ammoniated beet pulp; these materials might replace some of the protein in the diets of cows without serious interference with the production of milk or meat. It appeared that the bacteria of the rumen used the urea or ammonia as a source of protein, and were themselves digested in other parts of the intestinal tract. Mr. M. H. M. ARNOLD considered that more crucial tests of the value of urea should be made by giving it to cows receiving a diet low in pre-formed protein, and Sir JACK DRUMMOND, Scientific Adviser to the Ministry of Food, asked for reassurance that the urea would not pass into the milk.

Bacteria in the Synthesis of Vitamins

During the afternoon session Dr. S. K. KON of the National Institute for Research in Dairying, reviewing our knowledge of the part played by bacteria in the synthesis of vitamins in animals and human subjects, recalled that nearly 30 years ago the South African workers Theiler, Green, and Viljoen had concluded that the vitamin requirements of cattle were so low that they might be "covered indirectly by synthesis carried out by the extensive bacterial flora of the intestines." Eleven years later Bechdel and his colleagues in America showed that heifer calves could grow to maturity and reproduce on a diet which contained insufficient vitamin B to support growth in young rats for more than 2 to 4 weeks. When food was removed by means of a fistula from the rumens of cows which had subsisted for three years on the deficient diet, the partially digested material was now found to be a good source of vitamin B for rats. A bacterium of the genus *Flavobacterium* was, moreover, found in the rumen in profusion, and, when isolated and grown on a synthetic medium, proved to be a potent source of the vitamin B complex. Later experiments by other workers indicated that this bacterium and other microflora might be responsible for the synthesis of vitamin B_1, riboflavin, vitamin B_6, nicotinic acid, pantothenic acid, biotin, and vitamin K. Vitamin A was not synthesized, and must be included either as the pre-formed vitamin or as carotene in the diet of herbivora no less than of other animals. An interesting point had emerged in the study of the nutrition of ruminants in the first few weeks after birth. Until the characteristic bacterial flora was established the young animal must depend on exogenous supplies of the vitamin B complex. Thus nicotinic acid had been shown to be essential in the diet of very young calves.

There was ample evidence, Dr. Kon said, that the intestinal bacteria of ruminants were not alone in their ability to synthesize vitamins. A number of workers had demonstrated the presence of the vitamin B complex in the excreta of birds and of non-ruminant mammals, even when they were subsisting on a diet deficient in these vitamins. Recent work by Thompson had shown that *B. proteus vulgaris* could synthesize all known members of the vitamin B complex. Other intestinal organisms—*B. coli*, *B. lactis aerogenes*, *B. faecalis alcaligenes*, and *B. mesentericus vulgatus*—manufactured at least biotin, riboflavin, vitamin B_1, and nicotinic acid, while *B. coli* also produced vitamin K. In spite of the activities of these organisms, however, rats had been used successfully for 30 years in the estimation of several members of the vitamin B complex. It was obvious, therefore, that under normal circumstances the bacteria survived in the intestines or escaped into the faeces without, as in herbivora, yielding up all their vitamins to their host. The coprophagic habits of the rabbit might be significant. As found by Morot 60 years ago, and recently confirmed by Eden and others, this animal passed two types of faeces: during the day the faeces were hard and consisted of more or less completely digested food debris; at night the motions were soft, rich in protein, and swarming with bacteria. Unless precautions were taken these soft faeces were seized and swallowed by the rabbit direct from the anus. It seemed very probable that they represented an important source of the vitamin B complex.

"Refection"

Although rats could not usually subsist on diets deficient in the vitamin B complex unless they were allowed access to their faeces, they might sometimes grow and thrive if starch was included in the diet. This phenomenon, known as "refection," was first observed by the Danish worker Fridericia in 1926. A young rat, which hitherto had been losing weight on a diet deficient in vitamin B, suddenly picked up and began to grow at a normal rate. This change coincided with an alteration in the faeces, which were no longer dark brown and compact, but white and bulky through the presence of undigested starch. Further cases of spontaneous refection were soon reported from other laboratories. It was found that the condition could be transferred to other rats by allowing them to eat faeces from an infected animal. Dr. Kon said he had found that spontaneous refection occurred more often with potato starch than with rice starch. He thought that refection was not due to a specific organism, but that the presence of undigested starch and of the requisite starch-splitting organisms in the caecum led to vigorous fermentation and an acid *p*H, which favoured the formation of vitamins. Even in rats which had not "refected," however, it seemed probable that although the intestinal bacteria did not provide adequate supplies of all vitamins they at least made substantial contributions in some instances. This must be inferred from the need for additional vitamins in the diet when the bacterial activity in the intestines was suppressed by such drugs as sulphaguanidine and succinyl sulphathiazole. The vitamins affected included nicotinic acid, "folic" acid, biotin, vitamin K, and vitamin E, although we had no other evidence that vitamin E was synthesized by bacteria.

Experiments on Human Subjects

Summarizing recent work on the place in human nutrition of the synthesis of vitamins by the intestinal bacteria, Dr. Kon said that Oppel had shown that in human subjects on a uniform diet the amount of biotin excreted in the urine and faeces might be three to six times greater than the intake. In an extensive investigation by Najjar and Holt into vitamin B_1 nine adolescent males were given a basal ration free from the vitamin. At first small supplements were given, which were gradually reduced until the subjects had subsisted for some months on intakes of only 0.1–0.2 mg., as compared with the normal requirement of 1 mg. At this stage no clinical or laboratory symptoms of deficiency were noticed, except that the amounts of vitamin excreted in the urine were very low. When vitamin B_1 was omitted altogether four of the men developed definite symptoms of deficiency, including neuritis or oedema associated with anorexia and sometimes vomiting, within the following three to five weeks. In one man the symptoms were questionable, but the remaining four volunteers showed no sign of deficiency during seven weeks' observation. While only traces of vitamin B_1 were found in the faeces of those who showed signs of deficiency, much larger amounts were found in the faeces of those who had remained free from symptoms. The ability of the large intestine to absorb vitamin B_1 was demonstrated by a marked rise in urinary excretion after the injection of the vitamin per rectum. When one symptomless subject was given succinyl sulphathiazole the faecal output of vitamin was promptly reduced. Similar

experiments by the same authors had suggested that riboflavin also was synthesized in the alimentary tract. Ellinger, Coulson, and Benesch had found that the amount of nicotinic acid excreted by the human subject was often greater than the intake, and that the excretion was reduced after the administration of succinyl sulphathiazole. The pellagra-producing properties of maize might be due to its bad influence on the bacterial flora, since it was no worse than wheat (white flour?) in its content of nicotinic acid. Conversely the alleged ability of milk—a poor source of nicotinic acid—to prevent pellagra might be due to its good effect on the flora.

Dr. L. J. HARRIS, describing refection in rats in his laboratory, said that in the estimation of vitamin B_1 in bulky food materials the bradycardia method had the advantage of being very rapid, and thus did not allow time for the intestinal flora to be affected. Prof. FRIDERICIA mentioned that the starch recovered from the faeces of refected animals had recently been found to be less readily digestible than the original material.

Sir JOSEPH BARCROFT, F.R.S., recounted how, to confound sceptics, he had actually isolated 300 ml. of acetic acid from the intestines of a dead horse. Acetic acid was rapidly metabolized in a heart preparation perfused with Ringer's solution. In all herbivora about one-sixth of the digestible carbohydrate appeared to be converted to volatile acids in the course of metabolism. Dr. JAMES STEWART referred to the early work of Kellner, who had shown that, weight for weight, cellulose was about equal to starch in nutritive value. The symbiotic action of the bacteria of the rumen was therefore most efficient. The CHAIRMAN, in summarizing the proceedings, said that further work seemed desirable on the species of bacteria which were beneficial to their host. The influence of diet on the intestinal flora, and even on configuration of the alimentary tract itself, was an interesting subject. Thus it had been stated that the Russians, who were accustomed to bulky food, had large intestines of much greater capacity than those of the people of this country.

Correspondence

Health of Children in Wartime Day Nurseries

SIR,—Wartime day nurseries have now been open for some years, and doctors and nurses throughout the country have had an exceptional opportunity of observing the effect of a community life upon the health of these young children. Is it in the main a beneficial effect? Opinion seems to be divided, and there is little recorded evidence. May we therefore ask the hospitality of your columns to make known a scheme of research work which is being organized by the Medical Women's Federation into the health of children in wartime day nurseries compared with children of similar ages not in nurseries. The scheme falls into two parts. One part comprises an investigation by a whole-time clinician covering a comparatively small number of children but extending over a period of a year. This work is already being carried out by Dr. Margaret McLaughlin, on behalf of the Medical Women's Federation, in Birmingham, and we are greatly indebted to the medical officer of health and his staff in that city for making it possible to undertake this work. In the second part it is intended to compare the results of a single examination (relating especially to the evidence of respiratory infection) of a much larger number of nursery and non-nursery children throughout the country. For this the Federation will seek the co-operation of medical officers of health in many areas.

The purpose of the investigation is to obtain evidence which may have a bearing on the value of day nurseries, at least in so far as the health of the children is concerned, and which to that extent may be of assistance in determining future policy regarding day nurseries.—We are, etc.,

JANET M. CAMPBELL,
President, Medical Women's Federation.
KATHERINE M. HIRST,
Chairman, Day Nursery Committee.

73, Bourne Way,
Hayes, Bromley, Kent.

Episiotomy

SIR,—The article by Dr. J. D. S. Flew (Nov. 11, 1944, p. 620) and the subsequent correspondence are apt to be construed as an invitation, or even an exhortation, for the wholesale practice of episiotomy. If this procedure becomes almost a routine it can only add to the already ample, and seemingly inevitable, damage which results from childbirth.

I have no wish to offer carping criticism, and I feel sure Dr. Flew will absolve me from any such intention when, while agreeing with much of what he says, I maintain that his indications for episiotomy are too wide, and, moreover, are not convincingly supported by his figures. Apart from the "tone of the vaginal walls," why advocate episiotomy in the 58 cases out of 135 (a worth-while percentage) in which it was not found necessary? A torn perineum with a lacerated vagina is a nasty, unsatisfactory result, too often the finale of bad obstetrics and much to be condemned; but proportionately satisfactory, and the ideal often attainable, is the well-conducted normal primiparous confinement leaving an undamaged woman showing, two months later, practically no signs of childbirth.

I believe that few will subscribe to the idea of midwives carrying out this procedure at their discretion, even after special training. The most experienced can err in his judgment and make mistakes of omission or commission. The diagnosis of undue delay and its causation is often difficult; the arrival of the head on the perineum is not signalled in unmistakable fashion, nor is any satisfactory standard of measurement of uterine contraction possible. I know that these indications are not intended to be taken too literally, but one shudders at the possibilities envisaged if their interpretation were given to an even wider field than at present.

One other statement needs very conservative acceptance: the paraesthesia of the stretched perineum is very variable and has always been exaggerated. Even now one hears that "they even cut me before I got the chloroform." No episiotomy should be performed without adequate anaesthetic, nor is there ever need or excuse for so doing.

The importance of repair is rightly stressed by all; accurate apposition is essential for restoration of function and to avoid future discomfort. Particularly, as regards the latter, is this so at what will be the edge of the future introitus, where painful tags or scar are most likely. The vaginal floor is comparatively easy to suture correctly, but not so the perineal skin, especially as it nears its junction with vagina, and I need quite often to remove these stitches on account of puckering and begin again.

I would like to offer two methods which greatly facilitate the repair of an episiotomy. During a contraction, with the perineum stretched, make three or four transverse scratches with a needle, the first close to the mucocutaneous junction, covering the area to be incised. When it comes to sewing up, the needle is inserted and brought out in the line of each scratch mark successively; if the first skin stitch at the mucocutaneous junction is used to exert traction the remaining marks will be emphasized, and complete accuracy results. (No originality claimed.)

A second method is a little more bothersome. Hold the perineum on the stretch with two fingers in the vagina, insert the stitches between contractions before incising, clip the free ends, pass a narrow metal spatula under the loops on the vaginal floor, as a form of protecting guide, or produce them externally, and incise. A little practice soon obviates the annoyance of cutting the catgut loops, and the stitches can be tied directly the second stage is completed, thus avoiding any prolongation of the anaesthetic. Additional stitches are very easily inserted if required.

On the question of the anaesthetic, while any method can be made successful, I think that local analgesia should be reserved for the rare occasions when the attendant is without assistants of any sort. Less handling, less possibility of sepsis in an already injured tissue, less discomfort to the patient, and more freedom of action resulting in greater efficiency are my reasons for advocating general anaesthesia whenever possible.—I am, etc.,

London, W.1. F. NEON REYNOLDS.

Hypoproteinaemia during Recovery from Anaemia

SIR,—At the commencement of his article on hypoproteinaemia during recovery from severe anaemia (Jan. 13, p. 45), Dr. Trevor Davies writes: "Generalized oedema due to diminution of the serum proteins is not a common complication of the treatment of anaemia . . ."; and at the beginning of his comment he writes: "The above case illustrates the importance during the treatment of severe anaemia of maintaining a diet rich in protein."

In 1942 I published an article on the prevalence of hypochromic anaemia in the adult population. It may be of interest that since that time I have treated many cases of hypochromic anaemia with haemoglobin between 50 and 65% of normal, but I have never seen oedema either before or during treatment. I have treated groups of cases with ascorbic acid, vitamin B complex (B_1, B_2, B_6), and vitamin A, but in no group did the administration of vitamin have any influence on the Hb%. However, one invariable result of the administration of ascorbic acid (200 mg. per day) was an immediate and progressive increase in the number of red cells, without any effect on the Hb%. Finally, in no case of hypochromic anaemia have I found any diminution in the serum albumin or serum globulin either before or during treatment.

It seems probable that the condition, which continues to be prevalent in young adults of both sexes, is due to deficient intake of iron, but the deficiency is probably due to the low consumption of meat, and not the low consumption of vegetables as used to be thought.—I am, etc.,

London, S.E.24 KENNETH MCFADYEAN.

Bilateral Tuberculous Pleural Effusion

SIR,—Major Peter Kerley[1] states that double effusions are rare in tuberculosis, and Prof. Bruce Perry,[2] in his very interesting Bradshaw Lecture on the aetiology of erythema nodosum, states that a bilateral effusion is "an unusual occurrence with tuberculous effusion." This does not mean that bilateral exudative pleural effusion is rarely tuberculous, but may easily be so interpreted unless a clear warning is given.

Our experience of bilateral tuberculous pleural effusion at Sidcup can only be very briefly summarized here, and probably merits more detailed analysis, as the alleged extremely serious prognostic significance of bilateral effusions[3,4] has not been confirmed in this unit. Of a consecutive series of 601 notified cases of pleural effusion, 319 male and 282 female, 35 were bilateral, of which 17 were male and 18 female. With an incidence of nearly 6% it appears that even the statement that double effusions are rare in tuberculosis needs correcting.

In our series of 601 cases a history of erythema nodosum has been obtained only 15 times (2.5%), of which cases 10 were female and 5 male, with an age grouping between 15 and 29 years and a maximum incidence around 21 years. All these cases were strongly Mantoux-positive with a dilution of 1:10,000. In 6 cases there was an interval of about a year between the erythema nodosum and the onset of the pleural effusion.

A history of erythema nodosum is probably best elicited by asking every patient if he has had "rheumatism with red lumps on the legs" (it was a pleasure to read that in the San Joaquin Valley the people call erythema nodosum "the bumps"!), as patients have so often been told by their doctors that they have had rheumatism. So much does the "rheumatic" aetiology stick that in 1944 a boy of 18 years was subjected to tonsillectomy a few weeks after an attack of erythema nodosum in spite of a skiagram showing a grossly enlarged right hilum; he then developed a right pleural effusion and subsequently bilateral pulmonary tuberculosis, with positive sputum.

A useful investigation in cases of doubtful aetiology is the antistreptolysin titre, which will invariably be high in streptococcal cases; this investigation can easily be performed, while intradermal streptococcal tests are not readily available.

One final point: the Scandinavian authors have clearly shown that erythema nodosum is usually an *early* manifestation of tuberculous infection. This, although true in the majority of cases, is not always true. Two of my own cases prove it.

1. A girl aged 17 had been treated at the age of 8 for tuberculous glands of neck, developed erythema nodosum 8 years later, and after a further 12 months a tuberculous ascites and right pleural effusion.

2. A boy aged 18 had a laparotomy in April, 1944, for tuberculous ascites, then developed a left pleural effusion in July; tuberculin patch test was then possible. In November a cold abscess presented above the pubis and was found to originate from the right sacro-iliac joint. He had two crops of typical erythema nodosum before being transferred to a special orthopaedic unit. A skiagram of the chest showed complete resolution of the pleural effusion and clear lung fields. Antistreptolysin titre of serum was 30.

I wish to thank Dr. R. L. Quilliam for placing at my disposal some of his case notes. I also thank Sir Allen Daley and Dr. Ellingworth for permission to publish the figures.—I am, etc.,

Queen Mary's Hospital, Sidcup, Kent. E. MONTUSCHI.

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Nursing and Tuberculosis

SIR,—After reading Dr. Esther Carling's letter (Jan. 13, p. 59) it occurred to me that a useful investigation would be a tour of hospitals by a mobile mass radiography unit, and the nursing personnel filmed, those with suspicious films to be followed up in the usual way. This would establish the incidence of pulmonary tuberculosis in nurses, and a comparison could be made: (*a*) between general hospitals and hospitals for tuberculosis; and (*b*) with the general population. Certainly many of the factors that cause a breakdown with pulmonary tuberculosis are present while a student nurse is being trained.

In the same issue of the *Journal* Dr. Grenville-Mathers draws attention to the frequent failure to investigate home contacts of cases of pulmonary tuberculosis. I agree, and would add that the nursing personnel of sanatoria are contacts as much at risk as home contacts, and therefore should be re-examined and *x*-rayed periodically.—I am, etc.,

R. WRIGHT,
Coventry Medical Officer, Sterling Metals Ltd.

A Treatment for Superficial Eye Infections

SIR,—Wartime conditions, mainly "black-out" and working in a confined atmosphere, have created an increase in superficial eye affections. These excessive conjunctival vessel dilatations are painful, leading to worry and apprehension both to the patient and to his fellow workers, and absence from work.

The use of a solution of 1% natural ephedrine hydrochloride is not frequent in eye-drops, but I have found it useful to bring about decongestion of the conjunctival vessels. To this ephedrine solution can be added a weak solution of silver vitellinate, and enough sodium chloride to make the drops practically equivalent to normal saline. It is difficult to avoid the formation of silver chloride, but if the conjunctival sacs are irrigated afterwards with warm water from an undine the possible onset of argyrosis is reduced to a minimum; if a stable solution of the three above-mentioned components can be obtained the risk of argyrosis should be *nil*.

With the combined action of a decongestive and an antiseptic the eye is irrigated and disinfected simultaneously, while the patient gets early relief and is enabled to return sooner to work.—I am, etc.,

London, W.1. GRAYDON HUME.

Spinal Analgesia in Penetrating Abdominal Wounds

SIR,—I was much interested to read in your issue of Dec. 9, 1944 (p. 769), Major R. Binning's defence of a method of anaesthesia which I had hoped all careful and prudent surgeons and anaesthetists had long ago discarded. His assertion that it was the fact that a spinal anaesthetic was used in the case reported and not the Etherington-Wilson method of giving it which was the cause of death I most definitely refute. Although it is frequently taught that spinal anaesthesia is dangerous in cases of the acute abdomen, if properly used—as he can confirm any time he chooses to visit the Manchester School—it is perfectly safe. There is no doubt whatever that

the technique in the case quoted was the cause of death, as the analgesia had reached the lower cervical segments before respiratory paralysis occurred.—I am, etc.,

B.N.A.F. THOMAS MOORE.

Parotitis from Unusual Duct Obstruction

SIR,—I read the account of an interesting case of parotitis by Dr. R. H. Trinick (Jan. 6, p. 13). The following case of acute simple parotitis due to an unusual type of duct obstruction may be worth recording.

On Jan. 9, 1944, the patient, a male aged 55, attended the dental surgery at the West Riding County Mental Hospital, near Huddersfield. There was a large hard swelling of the left cheek which was causing a considerable amount of pain. The condition had been present for a week and was gradually getting worse. The left submaxillary lymph glands were enlarged and tender, and there was some difficulty in opening the mouth.

Examination of the teeth of the left side revealed no advanced caries. There was no inflammatory condition of the gums. A small amount of pus was noticed on the inner aspect of the cheek opposite the maxillary first molar. This was swabbed away, when the opening of Stenson's duct was seen to be enlarged and surrounded by a small zone of inflammation. I then noticed what appeared to be a small foreign body lying in the opening of the duct. Attempts to swab this away failed, and, on grasping the "foreign body" with a pair of dressing tweezers, a grass stalk of length approximately 2½ in. was removed from the duct. This was followed by the discharge of a small quantity of thin, yellow, fetid pus.

Irrigation of the mouth with a mild antiseptic solution was advised to keep the enlarged duct opening free from debris. The patient was seen again one week later. The swelling and pain had disappeared and the inner aspect of the cheek was quite normal in appearance.

It is remarkable that a stalk of grass of length 2½ in. could become completely embedded in the parotid duct, which has an average length of approximately 2 in. My thanks are due to Dr. D. K. Bruce, medical superintendent of the hospital, for allowing me to report the case.—I am, etc.,

Huddersfield. EDWARD I. FRIEND, B.CH.D., L.D.S.

Artificial Insemination

SIR,—I am distressed at the unrealistic attitude shown by many of your correspondents on this subject (copies of the *Journal* reach me two months late). Surveys before the war by Cattell and by Fraser Roberts showed that our national failure to reproduce was greatest among those who were above the average in their hereditary endowment for intelligence. For the past eighteen months I have been watching and doing my best to minimize the tragic preferential destruction of some of our best types—young officers and N.C.O.s of front-line infantry battalions. A similar selectively high death rate of the fittest, most courageous, and most intelligent is occurring in the other Services.

Soon this country will face a desperate shortage of types capable of leadership and of producing intelligent answers to novel and difficult problems. Temporarily we may tide over the crisis by ensuring that every child who has outstanding genetic potential gets the environmental chance to develop this potential. But this is living on genetic capital, and the future of our country depends on the rapid provision of new children born with high genetic potential for intelligence and other desirable qualities.

First and foremost, married couples who are themselves above the average must plan the size of their families to be above replacement level and above the average of the community. If, as Mr. Churchill thinks, the average couple should aim at four children, then the above-average must plan for six to eight. Secondly, "artificial insemination" should prove a most useful supplementary method of producing children of high genetic potential, since the male donors can be specially chosen for their superlative genetic endowment; for qualities where inheritance is by multiple genetic factors, as for intelligence, such children will have an endowment midway between that of the mother and the exceptional donor.

Artificial insemination should be used chiefly in two types of case. (*a*) Where a woman is unable to find a husband—there will be a considerable surplus of women over men of reproductive age after the war. In particular there will be numbers of young widows of good type, who have only been able to have one or two children before their husbands were killed. It is greatly in the national and their own interest that these women should have further children, at least up to the level of four, which would be replacing themselves and their dead husband. (*b*) In cases where the husband is sterile or should not father children for eugenic reasons, and both husband and wife prefer artificial insemination to the adoption of children. The use of a man's own sperms artificially to inseminate his wife when there is mechanical difficulty or relative insterility is clearly dangerous unless it is certain that the disability is not inheritable.

I am not competent to pronounce directly on the ethics of the matter; but ethical beliefs are subject to natural selection, according to the survival rate of those who hold them. A group or country which fails to avail itself of the possibilities of artificial insemination will have a correspondingly lower survival rate.—I am, etc.,

C. O. CARTER.

SIR,—The unimpassioned article on the practice of artificial insemination by Dr. Mary Barton, Mr. Kenneth Walker, and Dr. B. P. Wiesner (Jan. 13, p. 40) has come at a most timely moment. This is a straightforward procedure to be practised after due consideration on selected cases. One point, however, deserves further consideration—the registration of the birth of a child resulting from donor insemination (A.I.D.). In this matter I, too, have sought and quote eminent counsel's opinion: "In my view any husband or wife or medical practitioner who, knowing of the impotence or non-access of the husband, and knowing that the practice or operation of artificial insemination had been resorted to, wilfully gave information, etc., to the registrar that the husband was the father of the child conceived would commit an offence under the section. In the case of a title or inheritance being involved, questions of fraud or conspiracy to defraud the heir or other person entitled might well arise. In my opinion the only proper way to register the birth of a child conceived by artificial insemination is by leaving the columns for the name and other particulars relating to the father blank, whatever may be the subsequent embarrassment to the infant."

The advice, it will be seen, differs from that in the article, and, the possibility of disputed inheritance not being remote, it is the advice I give.—I am, etc.,

London, W. REYNOLD H. BOYD.

Deaf Aids

SIR,—It has recently been announced in the press that a Parliamentary investigation is shortly to be made into the subject of deaf aids. Perhaps my experience of these will be of interest and value to your readers.

Suffering from progressive deafness (otosclerosis) I have used aids of various types for more than 20 years, and until the war found these to be of increasing efficiency, especially after the introduction of the valve type of aid. During this time I have only once been the victim of a deliberate "ramp."

At the present time I possess three "aids," all of which *when in working order* are extremely efficient, even in my advanced deafness. The great snags now are keeping them in working order and the very high cost of maintenance. Aids A and B are of the same make, A being purchased shortly before the war and B in 1942. At first both gave excellent service and cost little more than the cost of batteries, as the jelly-type accumulators are charged at home, and a pair lasted two years. Both batteries and accumulators have since increased in price and depreciated in value. Below is a summary of the cost for repair and maintenance of A and B for the years 1943 and 1944.

1943	£ s. d.
January	5 5 8
February	14 0
April	1 0 8
May	8 0
June	16 0
November	1 7 6
	£9 11 10

1944	£ s. d.
March	3 0 0
April	4 4 0
November ..	1 9 6
December ..	8 15 1
	17 8 7
1943	9 11 10
Total ..	£27 0 5

Registered postage of instruments has been a heavy charge of which I have no record, nor have I any record of the cost of H.T. batteries, which last about 6 weeks and cost 6s. each

(plus postage). Both instruments are carefully handled and in no case was the damage due to violent usage (except in the case of valves damaged during return by post). This high cost seems to be due to the very poor quality of wartime components, the lack of skilled service mechanics, and the impossibility of getting the slightest adjustment made without sending the aid to London and risking postal damage.

In July, 1944, as both A and B were out of commission, I purchased aid C of another make at a cost of £26 5s. This, using only dry batteries, is light, compact, and very powerful, but is much more expensive to run, costing about 7s. a week in batteries only (purchase tax must be paid on some of these). In the four months since purchase four new valves have been required and a new switch. These have been supplied free under the guarantee, but are evidence of the poor material in use. In each case breakdown has meant a journey to Manchester (fare 7s.) and the waste of valuable time. The capital cost of my deafness in two years has been £53 5s. 5d. —maintenance £27 0s. 5d. plus cost of C £26 5s. In addition to this are running costs, of which I am now keeping a record, and the mental wear and tear of frequent breakdowns at most inconvenient times. Though many of these difficulties are due to the war, I feel that the following suggestions would be of help in tackling the prohibitively high cost of combating deafness: (1) The production of a "standard model" aid which could be serviced by any competent wireless mechanic and for which spares could be obtained by local wireless engineers. This would minimize damage in transit and need not interfere with the development of special models by individual manufacturers. (2) The development of light-weight accumulators, preferably of a type able to be charged at home, and of durable batteries. (3) Removal of the purchase tax from all batteries used for deaf aids. (4) Investigation of the possibilities of "all mains" sets, especially for home or office use, at a reasonable cost.

The heavy economic and social burden of deafness can now be greatly lightened for the well-to-do, but for many others expensive aids purchased in hope have had to be abandoned in despair because of the impossible cost of keeping them going.—I am, etc.,

Brierfield, near Burnley. E. M. BARLOW.

The Non-teaching Hospital in Planning

SIR,—In reference to your notice on the formation of an Association of Voluntary Teaching Hospitals (Jan. 13, p. 55) I should like to take the opportunity of stressing the importance of also obtaining comprehensive evidence from the so-called non-teaching hospitals in any planning or negotiations arising from the Goodenough report.

The hospitals without medical schools are responsible through their resident appointments for the practical post-graduate training of the majority of the general practitioners of this country. It would be interesting to know the exact figures, and I think that if these were obtained the result would be surprisingly high. The amount of clinical material available to each resident at these hospitals is usually greater than that available to a junior resident at a teaching hospital. In addition, a relatively junior resident at a non-teaching hospital is afforded greater personal responsibility than at a teaching hospital, and this is invaluable in after-life and equally important as the continuation of academic instruction at a hospital with a medical school.

It has always appeared to me that the value of these appointments has not been fully exploited by the medical profession. At the same time I think that to a certain extent the educational value is vitiated by the fact that the actual amount of work they entail leaves the residents with little, if any, time for concurrent study. The reason is frequently one of understaffing by the boards of management for reasons of finance, since they are naturally not interested in the question of higher medical education, but are only concerned with seeing that the work of the hospital is adequately carried out.

In view of the r educational importance I think there should be a proper survey of the conditions of these appointments, and, if possible, a register should be kept by a central authoritative body to which recently qualified men could refer, and which would be a guarantee that the hospitals represented on the register are adequately staffed, allow reasonable time for study, and provide all the necessary facilities. I consider that there should also be some differentiation of these appointments into those which are only suitable for men proposing to enter general practice and those suitable for men wishing to proceed to a higher qualification or gain a special diploma.

In view of the increasing number of medical graduates required, it is obvious that an even larger number of men will have to rely on these hospitals in the near future for their practical postgraduate instruction, and it is important that the best use is made of the vast amount of clinical material available. At the same time more generous staffing—both resident and consultant—of these hospitals would inevitably enhance the standard of work performed and thus benefit the population as a whole.—I am, etc.,

Bournemouth. THOMAS ROBSON.

Civilian Respirator as Anaesthetic Mask

SIR,—Dr. J. Morland Smith (Dec. 23, 1944, p. 820) rightly complained that the Clausen harness often obstructed respiration by depressing the jaw. I have not, as yet, tried his remedy with the wooden tongue depressor, but it has occurred to me that an anaesthetic mask of very similar design to the

ordinary civilian respirator would do much to overcome this annoying trouble. At any rate, this has been my impression with a converted gas-mask that I have been using for anaesthetic purposes during the past few months. If the correct size of mask is worn and the tapes are fairly tightly adjusted the jaw is well supported and has little or no chance of falling back throughout the anaesthetic. Furthermore, this type of mask keeps in position much more satisfactorily than the usual face-piece held by the harness, and the patient can be moved from trolley to operating table and into any position on the latter without much fear of the mask becoming displaced. With the gas in the bag at moderate pressure there is no leakage, and, when necessary, the mask can be removed and reapplied with ease and speed.

During the past three months I do not think I have had a single patient object to being so completely covered up, and all have been questioned before commencing the anaesthetic. The mask shown in the photograph is kept firmly attached to the plastic adapter by the elastic band found on the canister, and any size of mask can, if available, be used. To prevent sagging when the tubing is in position, narrow strips of plastic material have been inserted into small rubber sleeves at the sides and in front, below the window.—I am, etc.,

F. S. VAUGHAN,
Hon. Anaesthetist, County Hospital, Bedford.

Action of Eumydrine in Pyloric Hypertrophy

SIR,—In Sir Walter Langdon-Brown's fascinating address (Jan. 13, p. 35) mention is made of a subject that has long puzzled me. That is the use of eumydrine in infantile pyloric hypertrophy. The action of the vagus is generally given as that of an "emptier" and that of the sympathetic as a "filler." Now, as Sir Walter Langdon-Brown says, "atropine paralyses the vagus," and a few lines later that eumydrine, which has an atropine-like effect, is particularly useful in relieving pylorospasm. Surely its only possible action can be in abolishing the peristalsis of the stomach and so diminishing the vomiting. What is wanted is something that will paralyse the sympathetic.—I am, etc.,

Nelson. O. WILSON.

The Services

AMERICAN HONOUR FOR SIR E. M. COWELL

The President of the United States has awarded the military decoration of the Legion of Merit to Major-Gen. Sir Ernest M. Cowell, K.B.E., D.S.O., F.R.C.S., "for exceptionally meritorious conduct in the performance of outstanding services from September, 1942, to March, 1944," as director of medical services at Allied Headquarters, Mediterranean Theatre. General Cowell was responsible for the medical services of the Allied landings and later operations in North Africa, Sicily, and Italy. "He welded together the medical services of the American and British Forces and produced a highly successful organization which resulted in the saving of many lives and contributed to the well-being and comfort of the sick and wounded of both nations." He received the decoration at the hands of General Eisenhower on Jan. 15.

The following have been mentioned in dispatches in recognition of gallant and distinguished services in Italy: Brigs. (Acting) J. J. Magner, M.C., and J. G. Morgan, O.B.E., T.D.; Cols. (Temp.) C. B. C. Anderson, O.B.E., A. Angus, T.D., J. T. McOuat, O.B.E., T.D., R. M. Savege, O.B.E., M.C., C. H. K. Smith, O.B.E., M.C., J. R. N. Warburton, M.C.; Col. (Acting) G. G. Drummond; Lieut.-Col. J. H. Ward, D.S.O., M.C.; Majors (Temp. Lieut.-Cols.) W. A. Ball, T.D., W. S. Brindle, H. A. Brittain, J. D. Easton, O.B.E., W. Graham, L. J. Haydon, L. G. Irvine, D. MacD. Lyon, D. M. Mitchell, W. Patrick, G. W. Molyneux, E. F. S. Morrison, M.C., J. J. O'Connell, O.B.E., J. Pyle, M.C., J. H. Sangster, A. Wilcox, and P. H. Wood; Capt. (Temp. Major) (Acting Lieut.-Col.) N. G. G. Talbot; Major S. S. Chesser; Capts. (Temp. Majors) S. Alstead, A. H. Baker, E. L. Carter, F. A. Denz, J. F. Ford, E. M. Griffin, W. F. Hamilton, W. A. Heggie, M.C., C. C. Hurst, D. B. Jagger, D. Jefferiss, R. C. Little, J. C. MacKillop, B. J. Malley, D. Matheson, J. M. McKiddie, J. D. N. Nabarro, A. I. Ross, H. M. D. Shepherd, N. J. Y. Simpson, A. Stuart, H. Waters, W. R. West-Watson, M.B.E., J. H. Whittles, and E. G. Wright; Capts. H. Auger, E. Batley, O. H. Belam, C. Cameron, J. W. M. Christie, T. B. Davidson, K. B. Dawson, D. C. Devipe, G. F. Edwards, M.B.E., J. T. A. Essex, C. Giles, S. J. G. Gilmour, R. T. Grime, A. Henderson, A. W. F. Heron, E. W. Lindeck, J. G. Macarthur, M.C., D. Macdonald, J. McLean, L. F. McWilliams, F. E. Milson, A. E. Rampling, E. M. Sewell, J. M. M. Steven, M. G. Sutton, R. T. B. Watson, C. W. M. Whitty, and M. Wirtheim; Lieuts. C. Creffield, F. B. Lee, and R. C. Medland, R.A.M.C.; Capts. (Temp. Majors) L. N. O'Hara, A. K. M. Mazhar, and V. Parkash; Capts. S. C. Gosh, I. Singh, M. K. Ray, S. Kesavelu, S. K. Misra, and P. N. Swift; Subadar (Acting Subadar Major) H. Narian; Subadars M. K. Choudhury, B. N. Ray, and S. N. Lal; Jemadar B. H. Faroque, I.A.M.C.

The Cross of Merit (with Swords) has been conferred upon Acting Squad. Ldr. P. A Carrie, R.A.F.V.R., by the President of the Republic of Poland in recognition of valuable services rendered in connexion with the war.

CASUALTIES IN THE MEDICAL SERVICES

Died in Italy.—Capt. Michael Robert Mullins, S.A.M.C.

Wounded.—Capt. N. G. D. Campbell, War Subs. Capts. J. H. Bennett, S. M. P. Conway, M.C., J. C. F. Cregan, and J. Scott, R.A.M.C.

Repatriated in September, 1943, now known to be wounded.—War Subs. Capt. N. C. Rogers, R.A.M.C.

Reported missing at Arnhem, now known to be wounded and prisoner of war in Germany.—Major C. J. Longland, R.A.M.C.

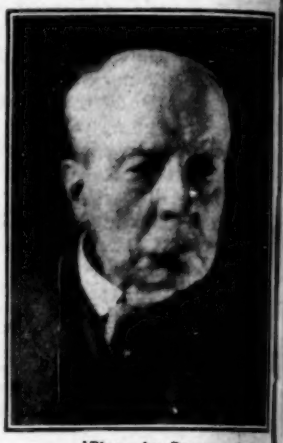
Missing.—Capt. B. d'E. Barclay, R.A.M.C.

Prisoners of war.—Lieut.-Col. W. C. Alford, O.B.E., R.A.M.C., Major C. Russell, M.C., R.A.M.C.

Obituary

SIR BUCKSTON BROWNE, LL.D., F.R.C.S.

The death of Sir Buckston Browne at the age of 94 removes a picturesque and attractive figure from his favourite haunts in Marylebone and Lincoln's Inn Fields. He retained a remarkable vigour till the end of his life. Buckston Browne belonged in spirit to a much later age than the mid-Victorian in which he was born, and physically too, for anyone listening to his strong voice and robust utterance would never have guessed his years. When he was 90 he announced his intention of living to be a hundred, and in token thereof renewed the lease of his Wimpole Street house for another ten years. At that same advanced age, after the second European war had broken out, he dismissed with contempt any suggestion that he should go to live in the country, and insisted on taking his usual walks in the "black-out." Within a few weeks of becoming a nonagenarian he addressed a public meeting on great athletic feats he had witnessed in his time, and famous pedestrians and pugilists who had been among his acquaintance. Their achievements he attributed to total abstinence, which he himself had practised for sixty years. His own particular "vanity"—to use a Wellerism which is appropriate with reference to one who was president of the Dickens Fellowship—was snuff, which he took as a prophylactic against colds in the head, but we believe he strictly rationed his allowance by putting the snuff receptacle in a distant part of his house so that some real effort was necessary if he wanted another pinch.



[Photo by Bassano, Ltd.

George Buckston Browne was born in Manchester and educated at Owens College. He was the only son of Dr. Henry Browne, physician to the Manchester Royal Infirmary and lecturer on medicine to the Medical School. Five successive generations of Brownes were doctors, the first of this line being Dr. Theophilus Browne of Derby, fellow-townsman and contemporary of Dr. Erasmus Darwin, grandfather of Charles Darwin, who lived in Derby from 1783 to 1802. George Buckston Browne was the fifth of this dynasty, and his great sorrow was that, having lost his only son, Lieut.-Col. George Buckston Browne, D.S.O., in the last war (he died in 1919), there was no one to follow him in the profession. But he found solace in the fact that his only daughter is the wife of Sir Hugh Lett, Past President of the Royal College of Surgeons.

In 1866, at the age of 16, Buckston Browne matriculated as a student of London University and entered University College, where he was presently awarded medals in anatomy, chemistry, and midwifery, gaining the gold medal for practical chemistry and the Liston gold medal in surgery. He qualified M.R.C.S. in 1874, and was made house-surgeon at University College Hospital, where he served under Sir John Erichsen, then at the end of his term as surgeon there, and was made demonstrator in anatomy under Prof. George Viner Ellis. Later he was invited by Sir Henry Thompson, then consulting surgeon to University College Hospital with a fashionable practice in Wimpole Street—he had just numbered the Emperor Napoleon III among his patients—to be his private assistant and afterwards his collaborator. He remained in association with Sir Henry Thompson for 14 years in private surgical practice in London, and then for 30 years he practised alone. His application to his profession was so complete that it was said that for 27 years he had neither a free day nor a holiday. When he was quite a young man the Harveian Society, which he joined in 1874, and of which after 50 years he was made Life President, honoured him by asking him to give the Harveian Lectures. The remuneration was not to be despised—15 guineas for three lectures—but the giving of those lectures had an immense effect on whatever success he had met with in his profession as a private surgical practitioner in London. Later in life he showed his gratitude by endowing the annual dinner of the Harveian Society and a biennial prize for essays by young practitioners.

Buckston Browne's Benefactions

The fortune which he acquired by addressing himself zealously to his work he used magnificently in the interests of the profession and of the nation. In 1927 Sir Arthur Keith made an appeal for the preservation of Down House in Kent, where Darwin lived for 40 years and where he died in 1882. Mr. Buckston Browne, as he then was, undertook immediately to make himself wholly responsible for buying the estate and establishing a fund for its upkeep. He acquired the home from Prof. Charles Galton Darwin, grandson of Charles Darwin, and transferred it under the most liberal conditions to the British Association as a national memorial. Certain of the rooms, particularly the old study in which *Origin of Species* was written, were furnished as nearly as possible as they were when Darwin lived in them. He also commissioned the Hon. John Collier to paint replicas of his well-known portraits of Darwin and of Huxley to be hung at Down House, and the house gradually became a repository of Darwinia.

In 1931 Buckston Browne followed this with another splendid gift of £100,000 to the Royal College of Surgeons "for the erection, endowment, and equipment of an institution where problems relating to surgery or the surgical treatment of disease should be investigated by research workers chosen by the College." A surgical research farm was established in the village of Downe, adjoining Down House. The foundation stone of this enterprise was laid by the late Lord Moynihan, who declared on that occasion that Mr. Buckston Browne took his place among those who might be regarded and honoured for all time as "immortal benefactors." In reply Buckston Browne spoke of his happiness in being able to bring the spirit of John Hunter alongside that of Charles Darwin. He also made the remark that when he was a student he could not walk for ten minutes in London without seeing some unhappy person whose face was scarred with smallpox, and now the pock-marked face was hardly ever encountered, thanks to the work done by one of Hunter's pupils, Edward Jenner, on a research farm like the one at Downe, though, of course, not to compare with it in equipment.

This by no means completes the list of Buckston Browne benefactions. One happy notion of his was to endow an annual dinner for the Fellows and Members of the Royal College of Surgeons. For this purpose he set aside a sum of £5,000, the interest from which was to provide a dinner on the College premises for one hundred persons, and he stipulated that one-half of the invited guests should be members of the College (he had been a member himself for over 30 years, the diploma of Fellow being conferred on him by the Council in 1926 in recognition of his services to surgery). Possibly his appreciation of the social value of a dinner arose from his early association with Sir Henry Thompson, whose "Dinners at Eight" (for 8 persons, with 8 courses, at 8 o'clock) were famous Wimpole Street affairs, attended on occasion by royalty.

Sir Buckston Browne also gave £2,000 to University College Hospital, and from his collection presented certain pictures and articles of furniture for the common room of the senior staff of the medical school. His recreation was the study and collection of pictures and objects of art generally. He was the discoverer of previously unknown portraits of John Hunter and John Wesley, and presented them respectively to the Royal College of Surgeons and to Wesley House, Cambridge. He also made presentations of works of art to the Victoria and Albert Museum, the National Portrait Gallery, and the Harveian Society. All that had to do with past times and manners engaged his interest, which was evidenced in various ways. For example, at one of the first of the Royal College of Surgeons dinners each guest received a souvenir in the shape of a model of a catheter found in the surgeon's house at Pompeii, and many other instances of the kind could be cited. He had literary tastes, too, and was extremely proud of the dedication to him by George Meredith of the novel, *Lord Ormont and his Aminta*, published in 1894. In a letter to Mrs. Lister in 1892 Meredith wrote: "I find myself next to rehabilitation by the surgeon. This was Buckston Browne, and no victim of sharp instruments could be in skilfuller or tenderer hands. He did his work perfectly, and I had difficulty in getting him to take his fee."

The Royal College of Surgeons made him a trustee of the Hunterian Collection, presented him with the Gold Medal, and placed his bust in bronze on the staircase at Lincoln's Inn Fields. In 1932 he received his knighthood. His regret was that his wife had not lived to share that honour with him. She had died after a devoted partnership of 52 years. They married in the year in which he entered medicine. In her memory he endowed two cottages for aged people and arranged other benefactions in her native village of Sparsholt in Hampshire, and also dedicated a bed in University College Hospital.

C. FERRIER WALTERS, F.R.C.S.

We regret to record the death on Dec. 24, 1944, of Charles Ferrier Walters, F.R.C.S., consulting surgeon to the Bristol Royal Hospital. The son of Thomas Walters, chartered accountant, he was born on Dec. 26, 1874. He was at school at Burton College, where his uncle, the Rev. Dr. Ferrier, was headmaster. Apprenticed for a short time to a dentist in Park Street, Bristol, he soon decided to become a medical student, and entered the Medical School of University College, Bristol, in 1895. He did his clinical work first at the Bristol Royal Infirmary and later at the London Hospital, qualifying M.R.C.S., L.R.C.P. in 1900. He obtained his F.R.C.S.Eng. in 1904, and in 1909 was elected assistant surgeon to the Bristol Royal Infirmary. In 1915 he was elected full surgeon, and from 1925 until his retirement in 1934 he was senior surgeon to the Infirmary. During the war of 1914–18 Walters rejoined the R.A.M.C.(T.F.) and went to France with a C.C.S. During the Somme battle of 1916 he was given charge of an advanced abdominal operating centre at Aveluy, a new departure in those days, where he did much good work which went far to persuade reluctant authorities that urgent surgery could and should be carried out in the forward areas. This experience coupled with his 25 years of active work at the Royal Infirmary rendered him most eminently suitable for the post of group officer to the Bristol area when the Emergency Medical Service came into being in 1939.

Walters (writes a colleague) was a man of irrepressible energy, always in a hurry to get to work, but in his operating unhurried. He was a sound general surgeon who devoted a good deal of attention to genito-urinary surgery. In his younger days he was a fine gymnast. Throughout his life he loved handiwork—from small carpentering jobs to house-building. These were his relaxations. Among other recreations came sailing and nature study. Yet with all his bodily activity he made time for most varied reading. He was a member of the Moynihan Surgical Club, president of the Bristol Medico-Chirurgical Society (1929–30), and president of the Bath and Bristol Branch, B.M.A. (1932–3). Walters was a loyal, friendly colleague and a good teacher. He married, in September, 1905, Miss Gertrude Popham, daughter of the Rev. J. K. Popham. Their family consists of one son, now serving in the R.A.M.C., and three daughters. We offer our deepest sympathy to his widow, his children and grandchildren.

ISABELLA DOUGLAS CAMERON, M.D.

Members of the public health service and of the dinner club of paediatricians and others whose common bond was an interest in child welfare will learn with regret of the death, in an Edinburgh nursing home on Jan. 10, of Isabella Douglas Cameron, M.D., D.P.H., M.R.C.O.G., who was for 25 years a valuable officer of the Local Government Board and of the Ministry of Health, where she had a large share in the pioneer medical administration work in the setting up of the Maternity and Child Welfare Services, her contributions to which were in some degree rewarded in 1937 by a unanimous invitation of the Council of the Royal College of Obstetricians and Gynaecologists to become a member of their College.

A woman of strong individuality, with imagination and a keen sense of duty, Dr. Cameron received her medical education at the Medical College for Women, Edinburgh, and graduated with distinction in 1898. In 1906 she obtained her M.D. degree for a thesis on "A Study of the Dietary of Several Halls of Residence for Students in Edinburgh"—a companion study to Prof. Noel Paton's work on the dietary of the working classes in Edinburgh. After holding resident appointments at the Crichton Royal Institution, Dumfries, the Children's Hospital, Sheffield, and the Infectious Diseases Hospital, Walthamstow, Dr. Cameron worked in the Cambridge University Laboratories and obtained the D.P.H. of that University in 1905. She then returned to her old school as lecturer in physiology and was also engaged in research work in the Laboratory of the Royal College of Physicians, Edinburgh, where one of the results of her labours was a valuable article on the methods of standardizing suprarenal preparations. One of the processes was subsequently adopted commercially. In May, 1906, Dr. Cameron was appointed medical officer to the Carnegie Dunfermline Trust, a pioneer body so far as Scotland is concerned in the medical examination, treatment, and systematic physical training of school-children. From this appointment she went to that of medical officer to the Edinburgh Provincial Committee for the Training of Teachers, and Dr. Cameron employed the vacations her appointment afforded to visit institutions devoted to the care, management, and treatment of infants and young children in Germany, Canada, and the United States of America.

She was one of the many children of James Cameron of Stanley, Perthshire. One of her brothers is Mr. J. F. Cameron, Master of Gonville and Caius College and lately Vice-Chancellor of Cambridge University. A sister was a distinguished student of mathematics under Prof. Chrystal of Edinburgh.

W. F. MENZIES, M.D., F.R.C.P.

Dr. William Francis Menzies, for 38 years medical superintendent of Cheddleton Hospital, Staffordshire, died suddenly at Radlett on Jan. 12, aged 81. Born at Halifax, Nova Scotia (where his father was then chief cashier in the Bank of Nova Scotia), he came to this country at the age of 12 and entered Fettes College. On leaving school he began the study of medicine at Edinburgh University, graduating M.B., C.M. in 1885 and B.Sc. and M.D. in 1888. He obtained the M.R.C.P.Lond. in 1891 and was elected F.R.C.P. in 1920. Immediately on graduation he took up psychiatric practice, and was a resident M.O. first at the Kent County Mental Hospital, Maidstone, and then for a longer period at Rainhill, near Liverpool. At the end of 1898 he was appointed medical superintendent of the newly established County Hospital at Cheddleton, near Leek. He retired from the post in August, 1936, owing to ill-health.

Dr. Menzies's great skill and knowledge brought him wide recognition. In 1920 he was elected president of the Royal Medico-Psychological Association, and he published a number of valuable papers on mental disorder and deficiency. He was also honorary consulting psychiatrist to the North Staffs Royal Infirmary and honorary neuropsychiatrist to the Stoke-on-Trent Orthopaedic Centre. He joined the B.M.A. in 1891, was secretary of the Section of Neurology and Psychological Medicine at the Annual Meeting at Exeter in 1907, chairman of the North Staffs Division 1932–3, and president of the Staffordshire Branch in 1934–5; he had also been president of the North Staffordshire Medical Society. From the time that Cheddleton Mental Hospital was opened Dr. Menzies collected round him as members of his staff a number of enthusiastic musicians and started an orchestra, which gradually grew until in 1934 members of the staff and friends living in the neighbourhood brought the strength up to nearly 70, the medical superintendent himself conducting it with great success.

SIR THOMAS BARLOW, BT.

R. H. writes:

By the death of Sir Thomas Barlow the father of our profession and its oldest and most honoured member has been taken from us; but "nothing is here for tears, nothing to wail or knock the breast," for he had long outlived the ordinary span of human life. I first got to know him when I had the privilege of serving as his house-physician at the Hospital for Sick Children nearly fifty years ago. He was then at the height of his busy consulting practice, and his ward visits were apt to be hurried, but one quickly came to admire the thoroughness of his clinical investigation, the accuracy of his diagnosis, and, above all, the kindness of his heart. To him the sick were never merely "cases" but suffering human beings requiring his sympathy and help, and to children especially his kindness and sympathy were always most shown. He had also the shrewd common sense of his native Lancashire along with its dry humour. I remember telling him some years ago how, when he was attending Queen Victoria in her last illness and the reporters were waiting at the gate of Osborne House for the latest bulletin, one of them wrote to his paper: "Our spirits rose when we heard that Sir Thomas Barlow had left," and how he chuckled over the joke. But although very much *persona grata* as a physician in the highest circles he was no mere courtier, and he once said, rather wistfully, that he would gladly give it all up and "practise in a dispensary amongst poor folk"; and therein spoke the real man. He had lived so long that latterly he had come to be merely a name to many of the present generation, and it was interesting at an international gathering of paediatrists in London a few years before the war to see the look of astonishment on the faces of many of the foreign visitors—as if they were gazing on one risen from the dead—when he was introduced as the Barlow of "Barlow's disease" and to hear the deafening ovation which followed. Now he is gone, but he has left an inspiring example of a life nobly and usefully spent and of a character entirely upright, simple, and sincere.

Sir ERNEST COWELL writes:

I was privileged to serve as the penultimate house-physician to Sir Thomas Barlow at University College Hospital. This was in the days when the physician made his own diagnosis and confirmed it by laboratory test or *x*-ray examination, which were only just becoming available. The student was taught to draw conclusions by examining the patient all over, noting his tone of voice and texture of the palms and even looking under the bed.

Sir Thomas was the soul of kindness. At the end of a demonstration on a patient, which might take an hour with a pause for hot milk in the middle, he would slip a sovereign in the sister's hand and say, "Poor soul, give her this." In the passing of this great physician the profession has suffered a great loss. It is up to the present and coming generations of doctors to remind themselves of his clinical method, and, as Sir Thomas was always doing, to strive to discover fresh truths.

G. H. writes: I would like to add a few random words to the memoir printed last week, though I only knew Sir Thomas Barlow in the latter part of his long life. We came together about one or two things, more particularly in forwarding the work of the Royal Medical Benevolent Fund, which was a cause he loved more than any other in old age. I also had the happiness of meeting him in the family circle at Wendover among his children and grandchildren with great-grandchildren in the offing. To have talked with the Nestor of our profession as he sat by the fireside, his hand cupped to his ear because of deafness and his Father Christmas face beaming with benignity, is a memory to treasure. Much has been written and will be written of his great service to medicine. He outlived all his contemporaries and many of his juniors, became a legend, and grew so old that time seemed to have forgotten him. The ceremonial idea of a 100th birthday on Sept. 4, 1945, made us wish that the veteran physician might survive a few more months and add a final decoration to the part he had played in medical history. That was not to be, and who can grudge him his rest? Thomas Barlow's work has fertilized our science and practice; his influence is incalculable, but we may be sure it goes on, passing from generation to generation, and we may doubt if the simple solid humble doctor himself ever imagined that that kind of immortality would be his.

Dr. EDWARD LESLIE HORSBURGH died at his home in Ryde, Isle of Wight, on Jan. 3. He studied medicine in Manchester and graduated M.B., B.S.Lond. in 1910 and M.D. in 1914. He was physician to King Edward VII Hospital for Officers at Osborne and medical referee to the Royal National Hospital for Consumption at Ventnor. During the last war he served as assistant adviser in pathology at the Calais base. Before settling in practice he had been house-surgeon and house-physician at the East London Hospital for Children, Shadwell, and senior house-surgeon at the Manchester Royal Infirmary. In 1929–30 he was chairman of the Isle of Wight Division of the B.M.A. T. T. H. writes: The untimely passing of E. L. Horsburgh will be mourned by many beyond the confines of his native Isle of Wight. Contemporaries in Manchester, London, and the old B.E.F. will recall his sparkling and vivacious personality—his *gaieté de cœur*, irresistible and unforgettable—and his genius for friendliness. It was my privilege to live with him as student, hospital resident, and Army doctor and to know his blithe spirit with a brother's intimacy. Latterly of necessity our ways diverged, but the occasional reunion found that spirit and our affection undimmed by the passing years. "Whom the gods love die young" may truly be said of Leslie Horsburgh, grey hairs notwithstanding. In any company he radiated mirth, hilarity, and good fellowship, for he was a superb raconteur and mimic, and a witty and trenchant conversationalist. Many a "mess" and many a fellow traveller "on life's common way" must remember his camaraderie with gratitude. In truth, his natural endowments were many and various. He could have excelled with ease in other less exacting and more spectacular fields than medicine had he so chosen. Golf, the stage, or letters might all have known him as a star, but he preferred to keep these as hobbies in his life's work as a physician. Who can doubt that he was right?—certainly not the crowded company of those by whom he was beloved as guide, philosopher, and friend. Even in his own profession he eschewed the limelight. His abilities would have carried him to the very front rank in pathology or clinical medicine. Instead he chose general practice. Again who shall criticize his choice? He was assuredly the ideal family physician—skilled, devoted, and always refreshing to the spiritually weary. Humbug he scorned; truth he diligently sought and cherished. Here was a man whom to know was to love and to love was great gain. He "shall grow not old as we that are left grow old."

Dr. ROBERT STEWART of Lytham, Lancashire, died on Jan. He studied medicine at St. Mungo's College, Glasgow, and afterwards in Manchester, taking the diplomas of L.R.C.P.&S.Ed. and L.R.F.P.S.Glas. in 1899; eight years later he obtained the D.P.H. of the Victoria Infirmary. Dr. Stewart belonged

the British Medical Association throughout his professional life; he took a keen but unostentatious interest in its work and was a diligent reader of the *Journal*. He attended and enjoyed many of the Annual Meetings, and was a member of the World Tour in the summer of 1935 when the B.M.A. met in Melbourne.

Dr. EDWARD SMALLWOOD, of Knight's Hill, West Norwood, S.E., died on Jan. 15 at King's College Hospital. He studied medicine at University College, Liverpool, and in London, took the L.S.A. in 1894 and the M.R.C.S., L.R.C.P. in 1901, and soon afterwards obtained the M.D.Brussels degree. He held various junior posts at the Royal Infirmary, Liverpool, before settling in practice at Norwood, where he became medical officer to the Home for the Aged Poor and visiting medical officer to the local children's hospital. During the last war he served as honorary physician to the Chelsea War Hospital, the Meynell Hospital for Officers, and the Lambeth Auxiliary War Hospital. Dr. Smaliwood joined the B.M.A. in 1889 and was a past president of the Norwood Medical Society.

A great personality has gone with the death of Dr. JANE LORIMER HAWTHORNE. She was one of the pioneers of sex education for the young and attempted successfully to tear down the veil of prurient mystery with which it had been enveloped. As a lecturer for the Alliance of Honour and the British Social Hygiene Council she had great success. A sense of humour helped her in this, as also did her power of ranging herself along with her audience. She was not a lecturer "telling people" but one of themselves discussing the matter. She positively welcomed interruptions, and would follow them down any by-way that her audience wanted. As medical officer to child welfare centres in the early days she was able to give information in a form acceptable to the working-class mother. Her views (as in all matters) were very definite, and those on the subject of dummies for babies overflowed on to the walls of her Canning Town clinic. It was not enough for her that a normal healthy child had been produced and that the mother had satisfactorily established breast-feeding; there was always a careful examination with a note on the involution or position of the uterus and the condition of cervix and perineum. New ideas were always being tried out: there was no fear of mental stagnation when Dr. Hawthorne was about. Ill-health had diminished her activities for some time, and a love of gardens and plants was added to her other interests. One could not be in her company without realizing a very remarkable, original, and many-sided personality.—L. M. P.

Dr. ERNEST WORLEY'S death, while a great loss to the B.M.A. as a whole, will be particularly felt at the meetings of the City Division. Every year (writes a colleague) he drew up a programme of monthly scientific meetings where the lectures were much appreciated and followed by good discussions. He was able to infuse informality and friendliness so that the youngest, shyest, and most retiring members were made to feel that their opinions were wanted. Those who had held office will long remember the dinners before the scientific meetings, where they had an opportunity of making personal contact with the lecturer. All this meant a good deal of organizing work, which was never shirked when medical work was heavy or when Dr. Worley might have been thought to be fully occupied as organizing secretary for the Centenary Meeting. Dr. and Mrs. Worley loved the Division, and the Division loved them.

C. J. de V. S. writes: To everyone who knew J. J. O'MULLANE, whether as friends or patients, his early death will cause much sorrow and leave behind a void it will be hard to fill. His great understanding and sympathy for those in trouble, his readiness to give a helping hand to whomsoever needed it, endeared him to all who came in contact with him. He had an outstanding sense of humour—a ready Irish wit which would often waft away the cares and troubles of his patients. For many years he suffered from indifferent health, but his insuperable energy and his indomitable courage made him carry on his practice, never sparing himself day or night to go to the aid of those who needed him. Although his practice was large he never failed to keep in touch with the latest advances in medicine, and his treatment was always the most modern. His knowledge of medicine was extensive, and if he had not felt his work lay in general practice he would have attained great heights. I have worked with him, and no words can speak too highly of him as a colleague. His early death at the age of 52 years has cut short the work he was doing in Plumstead—work in which his heart lay; but in the minds of all who knew him one thought remains above all: "He was a man."

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

The programme of lectures on science in the history of thought, to be delivered in Mill Lane Lecture Rooms at 12 noon, includes one on Saturday, Feb. 10, by Dr. A. E. Clark-Kennedy on medicine and the progress of thought. These lectures are open, without fee, to all members of Cambridge or London University or of Girton or Newnham College.

UNIVERSITY OF LONDON

L. S. Penrose, M.D., has been appointed to the Galton Chair of Eugenics tenable at University College. He has been attached since 1939 to the Provincial Department of Health, Ontario, Canada, and is also a physician at the Ontario Hospital, lecturer in psychiatry in the University of Western Ontario, and medical statistician for the Province.

C. Rimington, Ph.D., B.Sc., has been appointed as from May 1 to the University Chair of Chemical Pathology tenable at University College Hospital Medical School. Since 1937 he has been on the staff of the National Institute for Medical Research.

The following candidates have been approved at the examinations indicated:

M.D.—BRANCH I *(Medicine)*: James Marshall. BRANCH II *(Pathology)*: R. E. O. Williams. BRANCH IV *(Midwifery and Diseases of Women)*: G. C. Brentnall, E. Garland Collins. BRANCH V. *(Hygiene)*: Sarah C. B. Walker.

UNIVERSITY OF GLASGOW

A graduation ceremony was held on Jan. 13, when the following medical degrees were conferred:

M.D.—*Thomas Anderson, †H. W. Bowyer, †T. McM. Curran, R. D. Campbell.

M.B., CH.B.—A. R. Beaton, J. E Bennett, Katharine N. Brittain, D. F. Bruce, J. P. G. P. Burnie, A. C. Connell, M. S. Crawford, W. A. Crawford, J. L. Crichton, W. Cullen, W. J. A. Dobson, Agnes P. Downie, R. E. Evans, R. C. Forrest, J. Freedman, Arthur Jamieson, J. L. Kelly, L. Kennedy, W. I. Kenyon, G. J. Ker, R. Lindsay, R. McP. Livingston, Margaret J. MacArthur, J. B. Macmillan, T. P. Magee, S. S. Meighan, W. Napier,* A. J. Nelson, I. A. Porter, G. B. Prentice, Jean A. Purdie, J. T. W. Robertson, S. J. T. Robertson, Janette C. Russell, T. Smart, J. R. Smith, Raymond Smith, Rose K. Smith, Isobel D. Stewart, J. B. Stirling, F. H. Stone, K. J. Whitelaw, T. C. D. Whiteside, A. M. Williamson, Alexander Young.

* With honours. † With commendation.

The Brunton Memorial Prize was awarded to J. K. Watt as the most distinguished graduate in medicine of the academic year 1943–4, and the West of Scotland R.A.M.C. Memorial Prize to C. M. Ross as the candidate with the highest aggregate number of marks in surgery, medicine, and midwifery in the final examinations for the degrees of M.B., Ch.B., 1943–4.

UNIVERSITY OF WALES

THE WELSH NATIONAL SCHOOL OF MEDICINE

The following candidates have satisfied the examiners at the examination indicated:

M.B., B.CH.—*(Hygiene)*: D. Anthony, J. H. Edworthy, Hannah P. Evans, J. C. Ham, I. D. Jacobs, Jane W. James, D. G. Jones, D. O. Lewis, D. R. Lewis, W. T. Lloyd, Olwen V. Rees.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

A quarterly meeting of the Council of the College was held on Jan. 11, under the chairmanship of the President, Sir Alfred Webb-Johnson, who was warmly congratulated by the Council on the award of a baronetcy. Arrangements were made for the delivery of professorial lectures on anatomy by Prof. A. J. E. Cave and on physiology by Prof. John Beattie. The first course will begin on Feb. 19. It was reported that the trustees of the Prophit Trust had reappointed Dr. D. E. Lea of the Strangeways Laboratory, Cambridge, and had appointed Mr. Peter C. Williams of the Middlesex Hospital, Prophit Research Students.

It was decided to recognize the posts of first and second house-surgeon of the Royal Northern Infirmary, Inverness, for the six months' surgical practice required of candidates for the Final Fellowship examination.

Diplomas

Diplomas of Membership were granted to Flavia Z. L. B. James and H. B. Marsden.

Diplomas in Public Health, in Psychological Medicine, and in Laryngology and Otology were granted jointly with the Royal College of Physicians of London to the following candidates:

DIPLOMA IN PUBLIC HEALTH.—P. S. Jaikaran, H. G. Williams.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—P. Cassar, Louise F. W. Eickhoff, R. K. Freudenberg, G. W. Green, D. Jackson, P. D. Scott, L. M. Shorvon, G. D. F. Steele, E. Wellisch.

DIPLOMA IN LARYNGOLOGY AND OTOLOGY.—R. G. Boyd, A. S. Davidson, N. A. Punt, G. Snowden, P. A. Thorpe.

ROYAL COLLEGE OF SURGEONS IN IRELAND

Prof. W. N. Rae, Sc.D., Registrar of the Royal College of Surgeons in Ireland, Dublin, has received the following letter from Sir Alfred Webb-Johnson, President of the Royal College of Surgeons of England, dated Dec. 28, 1944:

"I beg to acknowledge with thanks the receipt of your letter of the 22nd instant enclosing a donation of one hundred guineas from the Royal College of Surgeons in Ireland to the fund for the restoration of my College. I shall be glad if you will inform the President, Vice-president, and Council of your College that this spontaneous gesture is very deeply appreciated by me and my colleagues on the Council of this College. The gift will always be remembered as a token of our friendly relationships and as an earnest of our cordial co-operation in the future."

Medical Notes in Parliament

Women Medical Students: Admission a Condition of Grant

Dr. SUMMERSKILL on Jan. 18 asked Mr. Willink to make a statement on the report of the Interdepartmental Committee on Medical Schools.

Mr. WILLINK replied that the committee recommended a comprehensive programme for the reform and development of medical education and research. Certain of the matters involved would require legislation. These the Government proposed to discuss with the bodies concerned. Apart from these the committee's recommendations were in the first place for the responsible educational authorities to study in framing their future policy. The Government accordingly invited universities, medical schools, and teaching hospitals to give the report early consideration. Recognizing the fundamental importance of medical education and research to the future of the country's health services, the Government accepted the principle of increased grants for the purposes of medical education and research to be distributed by the University Grants Committee through the universities to medical schools, postgraduate schools and institutes, and hospitals used for teaching and research. They also accepted the suggestion that for a limited period these additional grants should be separated from the block grants received by universities for their work as a whole. The amounts of grant to be made from time to time, whether for capital or for recurrent expenditure, would be determined after consideration in the light of the recommendations of the University Grants Committee and the general financial position prevailing. The Government shared the views expressed in the report on the importance of affording to women equal opportunities to those enjoyed by men for medical training and for obtaining postgraduate experience. They had therefore decided, as recommended by the committee, that future payments of grant to medical schools should be conditional on the adoption by the school of the principle of admitting a reasonable proportion of students of both sexes. They recognized that schools at present open to one sex only might need periods of varying lengths to adjust their arrangements to a co-educational basis. They therefore proposed that the University Grants Committee in consultation with the university authorities concerned should be charged with the responsibility of determining from time to time whether the action taken by each of these schools complied with the principle to the extent that is reasonable. The Government attached equal importance to the revision of the medical curriculum. Their acceptance of the principle of increased grants for medical education and research was dependent on the early completion of this process. They were glad to learn that, as recommended by the committee, the General Medical Council had already taken the initiative in the matter.

Deaf Aids Committee

Sir D. HACKING asked on Jan. 8 for the names of the members of the committee appointed to advise and assist the Medical Research Council in promoting research into electro-acoustical problems of design and application of instruments in alleviation of deafness.

Mr. ATTLEE: The members of the committee are as follows: Dr. W. G. Radley (chairman), Mr. E. J. Barnes, Sir Lawrence Bragg, Mr. N. Fleming, Dr. C. S. Halpike, Mr. L. C. Pocock, and Dr. T. S. Littler (secretary). The committee has formulated a detailed programme of research, and investigations in which physicists are collaborating with otologists and physiologists are in progress. The investigations will take some time to complete, and it is not anticipated that the committee will be in a position to make any recommendations before the end of the year.

Tuberculosis in Repatriated Prisoners of War

On Jan. 16 Miss WARD asked the Secretary of State for War whether he was aware of the dissatisfaction of relatives with the arrangements made for repatriated prisoners of war suffering from tuberculosis; and if he would consider these complaints with a view to an alteration of the present policy. Sir JAMES GRIGG replied: It is the policy of the Army to discharge soldiers suffering from tuberculosis as soon as possible so that if necessary they may enter civil sanatoria near their homes. Repatriated prisoners of war are given special consideration, but I am aware that there is sometimes delay in admission owing to pressure on accommodation. The Minister of Health has therefore set aside a number of beds in E.M.S. hospitals specially for Service patients awaiting transfer to sanatoria. This should materially help to remove any cause for complaint.

Miss WARD asked if Sir James Grigg would inform the Minister of Health that his arrangements were most unsatisfactory and ask him to improve them in the future. Sir JAMES GRIGG said he would certainly pass on the message, but whether he should do it in quite those truculent terms was a matter he would like to consider. Dr. SUMMERSKILL: In view of the fact that these men contracted the disease in the Army, can Sir James Grigg say why he is shelving his responsibility in this matter? Sir JAMES GRIGG: Because that happens to be the arrangement prescribed in the Army Regulations. The Army does not look after tuberculous patients. Patients discharged for disability in the Army are looked after, in the case of tuberculosis, by the Ministry of Health, and in the case of other diseases in Ministry of Pensions hospitals.

Distillation of Salt Water

On Jan. 16 Capt. STRICKLAND asked the Parliamentary Secretary to the Ministry of War Transport what steps had been taken by the Government to encourage research into the conversion of salt water into drinking-water by demineralization, evaporation, or other processes; whether any effective and convenient method had been evolved; and whether it was proposed to make the fitting of the necessary apparatus compulsory on all sea-going vessels, including their boats. Mr. NOEL BAKER said that the Government had done extensive research into the distillation of salt water by demineralization and evaporation, and apparatus designed by private inventors had been examined and tested. As a result two types of fresh-water producers for lifeboats were now issued on free loan to shipowners. A third and smaller pattern for use in emergency rafts was in production. Sea-going vessels carried adequate supplies of drinking-water for use on board. The filtering type as well as the distillation type was being used.

Medical News

A meeting of the Medical Society for the Study of Venereal Diseases will be held at 11, Chandos Street, W., to-day (Saturday, Jan. 27) at 2.30 p.m., when Dr. David Erskine will give an address on "Difficulties in the Successful Treatment of the Venereal Disease Patient."

Dr. Andrew Topping will speak on the "Aims of U.N.R.R.A. in the Health Field" at a meeting arranged by the Polish Medical Association in the U.K. to be held in the Hastings Hall of B.M.A. House, Tavistock Square, on Jan. 30, at 5 p.m. The lecture is open to all and will be followed by questions and discussion.

Prof. T. Wallace, D.Sc., will deliver two lectures on "The Diagnosis of Mineral Deficiencies in Crop Plants" before the Royal Institution, 21, Albemarle Street, W., on Tuesdays, Jan. 30 and Feb. 6, at 5.15 p.m.

The Science (Research) Society has arranged two public lectures. The first, on Wednesday, Jan. 31, at 6.45 p.m. in the City Literary Institute, Stukeley Street, Drury Lane, W.C., will be by Lady Eve Balfour, of the Haughley Research Trust, on "The Living Soil"; the second, on Saturday, Feb. 24, at 3 p.m. in the Hastings Hall of B.M.A. House, Tavistock Square, will be a technical discussion on "Soil Biology," by Lady Eve Balfour and Dr. E. W. Russell of the Rothamsted Experimental Station.

The Seventh Addendum to the *British Pharmacopoeia, 1932*, which was noticed in an annotation last week (p. 89) will be published on Feb. 1, and becomes official from that date. Constable and Co. Ltd., 10, Orange Street, Leicester Square, London, W.C.2, publish it for the General Medical Council.

Prof. F. Wood Jones, F.R.S., F.R.C.S., will give an address on "The Mammalian Toilet" before the Royal Institution, 21, Albemarle Street, W., on Friday, Feb. 16, at 5 p.m.

The following lectures will be delivered at the Royal Institute of Public Health and Hygiene, 26, Portland Place, W., on Wednesdays, at 3.30 p.m.: Feb. 7, Surg. Rear-Adml. G. Gordon-Taylor, "Surgery and Russia"; Feb. 14, Dr. G. H. Newns, "The Problem of Infant Mortality"; Feb. 21, Dr. I. H. MacLean, "The Problem of Whooping-cough Immunization."; Feb. 28, Dr. Harold Balme, "The Place of Rehabilitation in Hospital Service"; March 7, Lord Forrester, "Industry and its Environment—Physical and Social"; March 14, Mr. V. Zachary Cope, "Surgery in the Life of To-day"; March 21, Dr. Janet Aitken, "Rheumatism in Children"; March 28, Mr. Frederick W. Pratt, "Some Obstructive Abdominal Conditions in Infancy."

Field-Marshal Alexander has convened a medical conference, to be held in Rome at the end of the month, which will be attended by leading medical officers from the Allied Medical Services.

Orange-juice jelly, having a declared minimum content of vitamin C of 12 mg. per oz., will be available to school canteens, residential schools, etc., from Feb. 4, price 6½d. a lb. in cases of 42 lb. The average potency of the vitamin is expected to be about 17 mg. per oz. Local food offices will issue particulars of the scheme to the establishments concerned.

EPIDEMIOLOGICAL NOTES

Discussion of Table

In *England and Wales* during the week the incidence of measles rose steeply, 3,077 more cases being notified than in the previous week. Acute pneumonia, whooping-cough, and dysentery also showed increases, of 430, 359, and 81 respectively. There were 50 fewer cases of scarlet fever.

The rise in whooping-cough was general throughout the country and there were no large local variations in incidence. Yorks West Riding reported a fall of 52 in scarlet fever notifications. Those of pneumonia were the highest for a year, and in Lancashire, Warwickshire, and Yorks West Riding there were increases over last week's totals of 98, 51, and 50 respectively. Practically every county showed a substantial increase in measles: Warwickshire reported 415 more cases than last week, Lancashire 323, Staffordshire 321, Nottinghamshire 306, Cheshire 209, Yorks West Riding 193, Durham 131, and Middlesex 117.

Returns for dysentery in London rose from 16 to 67 (Wandsworth 44). The other large returns were those of Lancashire 24, Surrey 21, Yorks West Riding 13, Essex 11.

In *Scotland* measles notifications were 226 higher than last week, and whooping-cough 31, while the only disease to decline in incidence was scarlet fever, with 26 fewer cases than last week. The notifications of cerebrospinal fever, 37, were the highest in recent months; one-half of these cases were recorded in Glasgow. The largest returns of dysentery were Glasgow 37, Edinburgh 13, Lanark County 13, and Fife County 10.

In *Eire* a fall in the incidence of diphtheria reduced the notifications by 81, but the disease is still widespread: the 110 cases were reported from fifty areas.

In *Northern Ireland* infectious diseases were more prevalent. The increases over last week's totals were: Measles 93, scarlet fever 18, diphtheria 12, whooping-cough 8. In Belfast C.B. notifications of measles and whooping-cough rose by 100 and 8 respectively. Londonderry had 8 more cases of diphtheria than last week.

Quarterly Returns for England and Wales

During the September quarter the birth rate was 17.6 per 1,000 and was the highest rate for a third quarter since 1926. The birth rate in the third quarter of 1943 was 16.2, and the average for the third quarters of the preceding five years was 15.0. Infant mortality was 40 per 1,000 live births—below the average of the ten preceding third quarters. The diarrhoea death rate under 2 years of age was 6.4 per 1,000 live births, compared with 5.9, 5.2, 5.1, and 3.5 in the preceding four quarters. The stillbirths represented 2.7% of the total births registered. The general death rate was 10.3 per 1,000, compared with 9.4 for the third quarter of 1943, and with 9.9 for the average of the five preceding September quarters. The natural increase, excess of births over deaths, was 76,340, the corresponding figures for the third quarters of 1941–3 being 46,285, 71,000, and 70,833 respectively. There were 164,604 persons married in the quarter—an increase of 1,696 on the third quarter of 1943, but 76,408 below the five-years average.

Week Ending January 13

The returns of infectious diseases in England and Wales during the week included: scarlet fever 1,330, whooping-cough 1,678, diphtheria 459, measles 10,979, acute pneumonia 1,399, cerebrospinal fever 53, dysentery 302, paratyphoid 5, typhoid 5. Seventy-two deaths were attributed to influenza in the 126 great towns.

No. 1

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended Jan. 6.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1945					1944 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	49	5	37	2	2	92	2	28	12	2
Deaths		2	2				3	1		
Diphtheria	439	17	141	110	27	661	38	179	125	32
Deaths	14	—	—	1	1	22	2	5	5	1
Dysentery	204	67	110	—	—	165	22	37	—	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	—	—	—	—	—	1	—	—	1	—
Deaths		—					—			
Erysipelas			59	11	2			58	14	6
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				13					11	
Deaths	41	6	5	6	3	44	11	10	10	3
Measles*	11,947	240	697	10	281	515	82	43	82	3
Deaths	13	—	1	—	—	—	—	—	—	—
Ophthalmia neonatorum	63	6	14	1	—	64	6	15	1	—
Deaths										
Paratyphoid fever	1	—	—	—	1 (B)	4	—	1 (B)	1	—
Deaths	—	—	—	—	—	1 (B)	—	—	—	—
Pneumonia, influenzal†	1,242	60	14	2	20	1,608	140	79	44	6
Deaths (from influenza)	55	9	2	2	1	255	31	21	5	2
Pneumonia, primary			368	19				516	28	
Deaths		65		24	15		85		28	17
Polio-encephalitis, acute	2	—				1	—			
Deaths		—					—			
Poliomyelitis, acute	3	—	—	1	—	3	—	3	1	1
Deaths		—					—			
Puerperal fever		3	15		—		4	12		1
Deaths							—			
Puerperal pyrexia‡	124	10	11	2	—	147	11	13	1	5
Deaths		—								
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,462	48	192	18	67	1,791	108	220	37	87
Deaths	—	—	—	—	—	—	—	—	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	8	1	—	8	—	4	—	2	10	3
Deaths	—	—	—	1	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	1,538	80	84	72	19	1,793	195	121	76	25
Deaths	15	—	2	1	1	7	1	2	1	
Deaths (0–1 year)	480	54	72	43	35	425	75	120	61	26
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	6,796	1105	697	315	171	6,084	977	839	339	162
Annual death rate (per 1,000 persons living)			15·8	20·3	§			19·3	22·1	§
Live births	7,753	821	929	451	305	7,001	854	1,025	407	281
Annual rate per 1,000 persons living			18·6	29·1	§			20·8	26·6	§
Stillbirths	224	20	26			228	29	31		
Rate per 1,000 total births (including stillborn)										

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

‡ Includes puerperal fever for England and Wales and Eire.

§ Owing to evacuation schemes and other movements of population, birth and death rates for Northern Ireland are no longer available.

Letters, Notes, and Answers

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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ANY QUESTIONS?

Inheritance of Cancer

Q.—*What are the latest views on the inheritance of cancerous tendencies? Is there evidence to support the popular view that such tendencies are hereditary or familial?*

A.—Though actual proof is not an easy matter, there can be little doubt that heredity does play some part in the determination of neoplasms in the human subject. Such tumours as glioma of the retina, the neurofibromas of von Recklinghausen's disease, and polyps of the large intestine are hereditary beyond any doubt. But how large is the hereditary factor? This cannot easily be answered by statistical investigations on man; the generations pass too slowly, and errors of various kinds creep in. Cancer families have been described, and a mere statement of the observed facts is impressive. For example, in a family studied by Warthin there were 175 individuals in four generations of whom 41 died of cancer; 26 cases were of the gastro-intestinal tract and 15 of the body of the uterus. But in a disease so widespread as cancer the chance accumulation of cancer in one family may occur. We must therefore depend upon deliberate experiment in short-lived animals—e.g., the mouse—in which irrelevant elements can be bred out by brother-sister matings and the tendency or lack of tendency to cancer can be concentrated. Genetic investigations of this sort have proved conclusively that for certain cancers—especially mammary, lung, and bone tumours—heredity is an important factor in the genesis of cancer. In mammary cancer it has been proved conclusively that the inherited tendency to cancer, transmitted by male or female and therefore chromosomal in origin, added to the action of the hormone oestrone and a factor present in mother's milk of high cancer strains, are, all acting together, essential to the development of tumours of the breast.

Epileptic Fits in Theatre

Q.—*A patient aged 17 has had epileptic fits for two years. They occur only when he visits a theatre or cinema, and take the form of convulsions, biting of the tongue, incontinence of urine, followed by headaches, giddiness, and falling to sleep. He vomits after the fit. Recently he has bed-wetted. Physical examination reveals nothing abnormal. Although the fits seem to be those of idiopathic epilepsy, are they possibly functional, as they occur only in the circumstances described?*

A.—These are undoubtedly epileptic attacks. There is no suggestion that they are hysterical. In some patients epileptic fits arise in response to highly specific stimuli and in highly specific circumstances. It is usual to find that, although a special trigger will produce a fit, they also occur spontaneously, and it is likely that the recent bed-wetting is the result of unrecognized nocturnal attacks. The present story is interesting, though not remarkable, and at least the patient knows how to reduce the number of his attacks.

Recurrent Phlebitis

Q.—*A man aged 53, weight 14 st., is subject to frequent attacks of phlebitis chiefly affecting superficial veins. Eight years ago he had a large infarct in the lung. He is strong and healthy and does not appear to have any other disease. Can you offer suggestions about treatment?*

A.—To cause a recurrent phlebitis there must be a septic focus somewhere which "spills over" into the blood stream from time to time. The common foci are the nasal sinuses, the tonsils (especially if there has ever been a quinsy), and the teeth—either carious or dead, or dead and filled. As the man weighs 14 st. he may have gall-stones (a previous history of typhoid is occasionally present). The prostate may be the focus, and the urine should be examined for pus cells after a prostatic massage. The patient may be a diabetic with declared glycosuria; or hidden diabetes with no glycosuria but a high blood sugar may be found. The fact that the phlebitis is in the leg indicates diseased veins here, almost certainly varicose. The remedy, therefore, is to locate and eliminate the septic focus and to have the varicose veins treated by a surgeon expert in this.

Excessive Flatus

Q.—*A male aged 65 suffers from excessive flatus—so bad that he has to leave the room several times a day to expel it. Bowels act regularly with paraffin. At times the colon becomes so disturbed as to resemble megacolon under x-ray examination, which also reveals much spasm of the colon. There is considerable pain in the left loin—probably the result of the gaseous distension. Belladonna gives no relief. What treatment would you advise?*

A.—In later life absorption of gas from the bowel may be diminished owing to age changes in the blood vessels. Efforts should therefore be made to check the formation of gas from air-swallowing or fermentation in the colon. Excessive flatus is characteristic of intestinal carbohydrate dyspepsia, in which incompletely digested starch grains reach the colon and give rise to acid and gas there. Most authors attribute this to a disturbance of intestinal motility, and phenobarbitone, gr. 1/2 to 1 b.d., may be of value in checking hypermotility and spasm. A mucilaginous aperient such as psyllium seeds or one of the proprietary preparations thereof would probably be better than liquid paraffin. Potatoes and rice should be forbidden and takadiastase gr. 5 given at meal-times.

Control of Colostomy Evacuations

Q.—*A patient who had a permanent colostomy performed in May, 1944, has never been able to control the colostomy evacuations, which do not occur with reference to meals. I have tried allowing him one big meal a day, at midday, and thereafter fluids only. He has been given bismuth in a mixture, as well as tinct. opii, but to no avail. What do you advise?*

A.—The question does not provide enough information to enable a useful reply to be given. What was the type of colostomy: was it transverse or sigmoid colon which was used? What was the condition for which it was performed? Are the motions loose or merely erratic in their appearance? Answers to all these questions are necessary before an opinion can be given. A transverse colostomy is usually rather more difficult to control than a left iliac, owing to the difference in the consistency of the contents of these regions of the colon. Then, again, the original condition may be present proximal to the opening as well as distal—for instance, a secondary carcinoma or a widespread diverticulosis, and so on. Most colostomy patients find the secret of success lies in the establishment of a moderate degree of constipation; but while some rely upon this alone, others adopt a regular routine wash-out of the bowel twice a day. Either of these methods may be entirely satisfactory, and it is not possible to prognose which will be the better for any individual patient. Both should be given a trial. Of course, considerable modifications of the diet are often necessary to achieve the desired consistency of the motions, and because of the great idiosyncrasies of the bowel the patients usually find out for themselves what article of diet they must forgo.

Malaria and Pregnancy

Q.—*An English lady of 32 had malaria 12 months ago on the Gold Coast. She returned to England last July, and was free from attacks until the beginning of December, when she had two with two days' interval. She is expecting her second baby in February. How much quinine can safely be given to stop the attacks? Is mepacrine less dangerous? Is the baby likely to be infected with malaria? Her first baby was born 2 years ago on the Gold Coast, and she took 4 gr. quinine daily as a prophylactic during the whole time of her pregnancy without any ill effect.*

A.—Thirty grains of quinine daily may be given to stop the attacks of malaria if they occur, but in view of the possibility, so near term, of quinine's having some action on the uterus, mepacrine 0.2 g. thrice daily for 2 days, and then 0.1 g. t.d.s. for 5 days, would be preferable for this purpose. It would be infinitely better, however, to forestall relapse of the malaria by giving a suppressive course of mepacrine forthwith and continuing it for at least one month after parturition. One tablet (0.1 g.) daily should be taken throughout the period to achieve this end. The risk of the infant's being infected is negligible.

Fungus Infection of Toes

Q.—*A boy of 15 had a reddish rash with very small papules on the dorsum of his large toe, causing no pain or discomfort. This improved in the holidays with soaking in weak permanganate of potash. The condition has now spread to several other toes on the same foot. Is this a fungus infection, and what is the treatment?*

A.—A diagnosis may be made on inspection, or by the correct method of direct microscopical examination and culture with the object of proving the presence of ringworm fungus and the kind of fungus causing the infection. The second procedure is recommended, as otherwise the diagnosis rests upon guesswork.

Chemotherapy for Spastic Colitis

Q.—Having moderately severe spastic colitis, considered to be the late aftermath of an acute enteritis contracted some years ago, I was put on a 5-day course of a total of 30 g. of sulphaguanidine with marked benefit, followed by partial relapse a month later. I repeated the course with further benefit and lesser relapse. I should like to know the views on the toxicity of sulphaguanidine. What precautions apart from blood count are advised, and how frequently can such courses be repeated?

A.—Sulphaguanidine owes its action in the lower bowel to the fact that a large proportion of it is not absorbed at all; hence the blood levels attained are low, and, as would be expected, toxic effects are rare. The risk even of frequent repetition of the short course specified is very slight, and no special precautions are necessary except the cessation of treatment in the unlikely event of toxic symptoms being produced, such as fever or urticaria. The necessity for further repetition argues some degree of failure, and might be considered an indication for substituting succinyl sulphathiazole (sulphasuxidine); the degree of absorption of this drug is even less, and its antibacterial action in the bowel is somewhat more potent.

"Stress Incontinence"

Q.—A young girl, aged 23, who suffers from the distressing condition of urinary incontinence only in increased abdominal pressure, especially when laughing, is engaged to be married but dreads the day because of this complaint. There is nothing in the urine beyond phosphates. She is healthy. She has been tried with sedatives, ephedrine, and ergot, but to no avail. Is there anything in the fact that the uterine muscle is of the same structure as the sphincter? I should be glad of advice on the subject. If the line of treatment is ergot, how long should the treatment be kept up?

A.—Stress incontinence, believed to be due to a developmental weakness of the sphincter mechanism of the urethra and bladder neck, does occur in nulliparous women but does not usually manifest itself until later in life, when muscle atrophy sets in. It is rare in young girls, and in this case other causes should be excluded by careful investigation. Early organic nervous disease affecting the spinal cord, spina bifida occulta, a small pelvic tumour, lesions within the bladder or urethra—including developmental faults such as diverticulae, and a minor degree of epispadias which might not be noticed on inspection of the external meatus—are among the possibilities. Masturbation is also said to cause stress incontinence in young women. Apart from a thorough examination of the nervous system, examination under anaesthesia and cystoscopy may well be indicated.

If, after exacting inquiry, no other cause can be found, then a congenital or developmental weakness in the muscles and fasciae concerned in the control of the urethra must be assumed, and treatment is not easy. For stress incontinence due to obstetrical injury, various plastic operations on the bladder neck and urethra are carried out, but the results are by no means uniformly successful. In a case such as this, if the musculature is inherently weak then such operations would be even less likely to be successful, and something in the way of a fascial transplant from the abdominal wall to form a sling round the urethra might be required. It is difficult to say whether operative treatment is indicated here; it depends how troublesome the incontinence is, how often it occurs, what part is played by anxiety and loss of confidence, whether the patient intends to have children—and if so it might be more opportune to deal with it when the incontinence has been made worse—as it is likely to be—by childbearing. Unless the loss of bladder control is frequent and really troublesome, treatment on more general lines seems preferable, at any rate for the moment.

The patient should be told to pass urine frequently and to avoid a full or distended bladder. Contrast baths might help to tone up pelvic musculature, but, above all, pelvic-floor exercises should be tried. The urethral sphincters are assisted by the "accessory sphincter muscles"—i.e., the levatores ani and other muscles of the pelvic floor—and these might be trained to compensate for the weakness of the involuntary structures. Calcium and nux vomica are advised, but drugs are not likely to improve matters. Ergot in the form of the liquid extract was advised by some of the older writers. If it has any action on the involuntary sphincters, then presumably it is by reason of its alkaloids, ergotoxine or ergotamine, which have a stimulating effect on plain muscle supplied by motor sympathetic nerves. But recent workers suggest that the involuntary sphincters of the urethra are controlled by parasympathetic rather than sympathetic nerves, and in any case it is difficult to see how contractions resulting from ergot could have any lasting effect on the incontinence. Moreover, since ergotoxine and ergotamine are both liable to produce gangrene, they could not safely be given for more than a few days at a time.

It is not clear what is meant by the statement that the uterus and the urethral sphincter are of the "same structure." There is not a single sphincter in the female, but rather a sphincter mechanism which is complex and by no means fully understood. The internal and external sphincters are composed of involuntary muscle, the latter being of little significance. Between the two is the compressor urethrae, which is at least partly under voluntary control. To these must be added the fibromuscular fascia and ligaments lying beneath the anterior vaginal wall and around the urethra and bladder neck, and the accessory sphincter muscles of the pelvic floor; the length and direction of the urethra and the position of the bladder in the pelvis also play a part. It is not possible to compare a system of this kind with the uterus, and the only comment which might be made is that if this patient's incontinence is due to developmental weakness of the musculature of the urethra and surrounding parts, then the supports of the uterus and vagina may be similarly affected and she is perhaps predisposed to prolapse.

Treatment of Undulant Fever

Q.—One of my patients, a man aged 53, has had undulant fever for 4 months. After 6 weeks the agglutination reaction of Brucella abortus was positive to a titre of 1:1250. His temperature still varies from 99° to 101° F. I understand that T.A.B. vaccine given intravenously is sometimes useful in cutting short the pyrexia. I shall be grateful for any information regarding this, or any other form of treatment, with details of dosage, etc.

A.—Protein shock with T.A.B. vaccine has been used with some measure of success in undulant fever. It is usual to give three intravenous injections containing 25, 50, and 100 million organisms at 4 to 5 day intervals, but dosage will depend on the degree of pyrexial reaction to the first injection. A course of sulphonamide is sometimes effective, but it should not be continued beyond 10 days without white-cell counts. Another drug that has been recommended for undulant fever is "fouadin" (stibophenum) injected intramuscularly: the dosage is 1.5 c.cm. on the first day, 3.5 c.cm. on the second day, and then 5 c.cm. on alternate days. However, this patient's illness has already lasted 4 months and is likely to terminate spontaneously at any time now (the average duration of abortus fever is 10 weeks), so that it is doubtful if any heroic measures should be instituted at this stage.

A Case of Eunuchoidism

Q.—A well-developed and otherwise healthy boy of 17¼ was brought to me because his voice had not "broken." He had no sign of hair on the face. Pubic hair was, with the exception of two or three downy hairs, also absent. Penis was diminutive, and scrotum atrophic and empty. No sign of presence of testes anywhere was obtained. A course of gonadotrophic hormones was begun at once without result. What further treatment is indicated?

A.—The failure to respond to gonadotrophic hormones suggests that the primary disorder is gonadal and not pituitary, the diagnosis therefore being eunuchoidism. It seems improbable that one could produce gonadal development in this case; but secondary sexual characteristics would be developed, or maintained, by androgens. These could be given in three forms: (1) injections of testosterone propionate, 25 mg. twice weekly for 6 or more weeks; (2) methyl testosterone, 5-mg. tablets dissolved under the tongue, 1 t.d.s., for similar periods; (3) the implantation of 6 testosterone propionate pellets, 100 mg. each pellet, in the subcutaneous fat of the abdominal region, the effect lasting some 8 months. On cessation of therapy, in all methods, there is a tendency to regression, but not complete. Nevertheless, the therapy is substitution therapy, and has to be carried out continuously or intermittently if remission is to be avoided.

As to the question of the undescended testicles, even if the condition is primarily of pituitary origin, descent will not be obtained by the administration of hormones should the testes be ectopic and mechanical anatomical obstruction be present. Occasionally cases have been described, of similar character to the present one, in which the gonads unexpectedly turned out to be ovaries or ovo-testes.

Sleep-walking

Q.—A girl aged 14, normal in every respect, recently walked in her sleep. She dreamt she was going for a walk through a window. She climbed out of the window of her bedroom, and dropped 20 ft. on to the stones below, fracturing her spine. She is known to have walked in her sleep only once before. She is a stable girl, with apparently strong nerves, and not upset by such things as bombing, etc. What precautions could be taken against a repetition of the above?

A.—Sleep-walking (like dreams) is a sign of an unresolved problem: in psychological language it is a case of "perseveration"—i.e., the tendency of the mind to revert to an unfinished train of thought. In ordinary language we call it "worry"; but in sleep-walking the worry has been repressed and has become dissociated and therefore acts automatically. Usually in a dream the attempt to work out the problem takes place purely subjectively, and without discharging itself in any motor path. But occasionally the problem is so urgent and vivid that, as in the case of Lady Macbeth, it discharges itself in action, and this action takes the form of re-enacting

the original unresolved problem to try to find a solution. The dream helps us to discover what that problem is. Obviously the only satisfactory way of preventing a recurrence in this girl is to find out what that problem was, or is, and for this a really good medical child-psychologist should be consulted. It is quite usual for those having subjective problems and anxiety to be free from objective fear, as of bombs, and also to appear perfectly normal in behaviour.

Vitamin C and Hay-fever

Q.—*I have seen it stated that hay-fever has been cured or greatly alleviated by large doses of vitamin C—up to 500 mg. a day. The authority quoted is Dr. Holmes, president of the American Chemical Society, 1942. Has this investigation been followed up, and where is further information obtainable?*

A.—It was claimed by Holmes (*Southern Med. Surg.*, 1943, **105**, 56) and Holmes and Alexander (*Science*, 1942, **96**, 497) that vitamin C in doses of 200 to 500 mg. daily is effective in the treatment of hay-fever. The clinical trials, however, were not adequately controlled, and in Holmes's series conclusions were based on the study of only 25 patients. Strict control is essential in all studies on allergy. Other workers have failed to substantiate the claims made for vitamin C in the treatment of hay-fever (*J. Amer. med. Ass.*, 1939, **112**, 662; *J. Allergy*, 1944, **15**, 236).

LETTERS, NOTES, ETC.

"Skiagram"

Dr. H. CLEMENT SIMCHOWITZ (Guildford) writes: With reference to this matter may I be allowed to correct the quotation of Roentgen's paper in the letter from your correspondent (Dec. 23, p. 833), who, rightly, points out that Roentgen's discovery of *x* rays was not a "stumble" by "accidentally fogging a plate" but the result of systematic experimental research while professor of physics at the University of Wuerzburg, Bavaria. Roentgen's original paper, "Eine neue Art von Strahlen" (a new kind of rays), a copy of which is in my possession, was published in the *Sitzungsberichte der Physikalisch-medizinischen Gesellschaft zu Wuerzburg* (Proceedings of the Wuerzburg Physico-medical Society), December, 1895.

Payment of Doctors in Mental Hospitals

"A.M.O." writes: The letter in the *Journal* of Oct. 28, 1944 (p. 579), raises a matter which should be of paramount importance to medical officers in mental hospitals. A matron in a large hospital may now receive £600 salary and, in addition, emoluments valued at £200. The average salary of a medical officer is £400 to £500. The cost of qualifying in medicine is now about £1,500. Substantial increases in remuneration have been received by the nursing and clerical staffs. This service may become even less attractive to medical men unless the scale of salary is raised and the conditions in general improved.

Headache and "Acute Abdomen"

Mr. D. G. WILSON CLYNE (London, W.1) writes: I was interested to read the note from Dr. T. L. Crawhall (Jan. 13, p. 70) on headache in relation to the acute abdomen. The crux of the whole matter seems to be the exact meaning of the expression "acute abdomen." If one considers acute salpingitis to be a localized type of acute abdomen, then I cannot agree with his aphorism, "An acute abdomen with a headache is never an acute abdomen." During the first two years of the war I was called upon to perform all emergency operations in a large county hospital as an E.M.S. surgeon. This departure from my normal type of work gave me ample opportunity of noting the incidence of headaches, particularly in relation to acute appendicitis. I entirely agree with Dr. Crawhall's aphorism in so far as it applies to this condition, and would even go further and state that on no occasion in a large series of acute appendices did I encounter headache as one of the cardinal symptoms. This cannot be explained by the fact that I omitted to question the patients as to the presence or absence of this symptom; the contrary was the case. In gynaecological practice I have often been impressed by the frequent association of headaches with both salpingitis and pyelitis, and some time in the past I think that I must have encountered another aphorism which runs rather like this, "Abdominal pain and headache in a woman, of acute onset, suggest that she is suffering from either pyelitis or salpingitis." I have repeatedly found the presence of headache of value in the differential diagnosis between salpingitis and appendicitis, and would even say that there is only one really common acute abdominal condition with which headache is often frequently associated—namely, salpingitis. In fact the presence of headache in a woman with an "acute abdomen" should make one consider very carefully before performing a laparotomy.

Coarse Tremor in the Elderly

Dr. W. N. LEAK (Winsford) writes: In "Any Questions?" (Jan. 13, p. 67) your contributor says: "I cannot suggest any medicinal treatment which will help these patients"—i.e., elderly people with a coarse tremor. In 1935 (*Journal*, **1**, 1097) I mentioned that prominal might "possibly find its most distinctive use in the control of tremors of various sorts, for many of which there is at present no effective medication." Experience since then has confirmed my opinion, and in the coarse tremor of the aged prominal (phemitone) sometimes produces dramatic improvement. For example, an aunt of mine, who could barely manage to drink her tea using both hands, within a week of commencing prominal was pouring out tea with one, to her great satisfaction.

Peptic Ulcer

Dr. P. K. MUSPRATT (Pleasington) writes: There appear to be many contributory factors in the aetiology of peptic ulcer, but I should like to stress one which is often ignored—namely, the ingestion of over-hot liquids. Digestive trouble is particularly prevalent among bus drivers and conductors, and I suggest that this may well be due to their consuming very hot tea which they have to drink quickly owing to the short time they have at the terminus. As the drivers appear to suffer more than the conductors the sedentary nature of their occupation may play some part. Women probably have more time and therefore drink their tea when it is cooler, especially as they take, as a rule, more sugar and milk, which cool the tea. The discomfort resulting from hot fluids is often not associated with its true cause, as it comes on a considerable time afterwards and is often associated with a feeling of faintness. I do not, of course, minimize the other contributory causes such as tobacco, alcohol, and perhaps the fumes from gas-fires with no chimney outlet, which escape into the room.

Mental Hospitals

Mr. J. P. SPENCER WALKER (Hove) writes: Dr. Otho FitzGerald (Dec. 2, p. 744) objects to the word "asylum," preferring mental hospital. He states that such institutions "are no longer merely places of rest and detention but provide active and specific forms of treatment." The word "asylum" is a beautiful word meaning sanctuary or place of refuge, and the word "hospital" means a place for the reception of guests, but neither in their original sense had anything to do with medical treatment—for example, St. Mary's and St. Bartholomew's Hospitals at Chichester. The former is still an almshouse, and so was the latter until recent times. The change from "asylum" to "hospital" was made owing to the debasing in the public mind of the former word.

Sensitiveness to Strychnine

Surg. Lieut. CAREY BAKER, R.N.V.R., writes: Dr. D. R. C. Shepherd's account of his case of sensitiveness to strychnine (Nov. 25, p. 694) recalled to mind a similar happening in my own experience. A married woman aged 36, a cook by practice, had been under my care for a week suffering from a heavy cold. On returning to work she felt rather listless and asked for a tonic. I gave her a mixture of iron and strychnine containing two minims of liq. strych. hyd. to the dose. I also was hastily summoned to find the patient collapsed, cold, pale, and almost pulseless within ten minutes of taking the first dose. Though I was sceptical about the attack being due to such a small dose of strychnine I could discover no other cause and was not prepared to experiment further. There was no previous history of sensitivity to the drug, but then, as the patient said, she seldom had to take any medicine. Fortunately no ill will was felt, the patient quickly recovered, and was given a strychnine-free mixture.

Gauze Impregnated with Paraffin

Messrs. JOHNSON AND JOHNSON (Great Britain) LTD. write: We would draw attention to the article which appeared on page 856 of the *B.M.J.* of Dec. 30, 1944, entitled "Curtain Net Impregnated with Paraffin." This product was manufactured by us for many years under the name "porowax" gauze, and was demonstrated extensively on several occasions at the London Medical Exhibition and on one occasion at the British Medical Exhibition. It was listed and illustrated for several years in our catalogue, and we would be grateful if due acknowledgment could be made to these circumstances in your *Journal*.

Corrigenda

The duration of pregnancy in three of the cases of "A.I.D." reported in the *Journal* of Jan. 13 (p. 43) is given as "45 weeks." The sentence should, of course, read "terminated successfully at 35 weeks."

The medico-legal note headed "A Fatal Overdose of Carbachol" published on Jan. 13 stated, incorrectly, that the report of the inquest appeared in our issue of July 4, 1944. The date should have been July 4, *1942* (p. 28).